MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2004 vocabulary. See http://www.nlm.nih.gov/mesh/ and http://www.nlm.nih.gov/pubs/techbull/nd03/nd03_mesh.html for a description of changes.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> fil embas

FILE 'EMBASE' ENTERED AT 13:34:24 ON 13 DEC 2004

FILE COVERS 1974 TO 9 Dec 2004 (20041209/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> fil biosis

FILE 'BIOSIS' ENTERED AT 13:34:27 ON 13 DEC 2004

FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 9 December 2004 (20041209/ED)

FILE RELOADED: 19 October 2003.

=> fil wpix

FILE 'WPIX' ENTERED AT 13:34:30 ON 13 DEC 2004

FILE LAST UPDATED: 8 DEC 2004 <20041208/UP>
MOST RECENT DERWENT UPDATE: 200479 <200479/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE, PLEASE VISIT:
http://www.stn-international.de/training_center/patents/stn_guide.pdf <<<

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE http://thomsonderwent.com/coverage/latestupdates/ <<<

>>> FOR INFORMATION ON ALL DERWENT WORLD PATENTS INDEX USER GUIDES, PLEASE VISIT:
http://thomsonderwent.com/support/userguides/ <<<

>>> NEW! FAST-ALERTING ACCESS TO NEWLY-PUBLISHED PATENT DOCUMENTATION NOW AVAILABLE IN DERWENT WORLD PATENTS INDEX FIRST VIEW - FILE WPIFV.
FOR FURTHER DETAILS: http://www.thomsonderwent.com/dwpifv <<<

>>> NEW DISPLAY FORMAT HITSTR ADDED ALLOWING DISPLAY OF HIT STRUCTURES WITHIN THE BIBLIOGRAPHIC DOCUMENT <<<

FILE 'REGISTRY' ENTERED AT 13:34:17 ON 13 DEC 2004
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PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 12 DEC 2004 HIGHEST RN 796841-97-9
DICTIONARY FILE UPDATES: 12 DEC 2004 HIGHEST RN 796841-97-9

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> fil hcap

FILE 'HCAPLUS' ENTERED AT 13:34:19 ON 13 DEC 2004
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PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 13 Dec 2004 VOL 141 ISS 25
FILE LAST UPDATED: 12 Dec 2004 (20041212/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> fil medlin

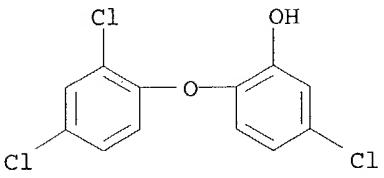
FILE 'MEDLINE' ENTERED AT 13:34:22 ON 13 DEC 2004

FILE LAST UPDATED: 9 DEC 2004 (20041209/UP). FILE COVERS 1950 TO DATE.

On February 29, 2004, the 2004 MeSH terms were loaded. See HELP RLOAD for details.

OLDMEDLINE now back to 1950.

CN Yujiexin
CN Zilesan UW
FS 3D CONCORD
DR 164325-69-3, 112099-35-1, 88032-08-0, 261921-78-2
MF C12 H7 Cl3 O2
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DIOGENES, DRUGU, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IMSDRUGNEWS, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PIRA, PROMT, PS, RTECS*, SPECINFO, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)
DT.CA CAplus document type: Conference; Dissertation; Journal; Patent; Report
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.NP Roles for non-specific derivatives from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2124 REFERENCES IN FILE CA (1907 TO DATE)
41 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
2130 REFERENCES IN FILE CAPLUS (1907 TO DATE)
2 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

=> => fil lreg

FILE 'LREGISTRY' ENTERED AT 13:34:15 ON 13 DEC 2004
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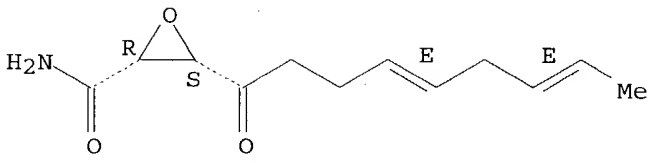
LREGISTRY IS A STATIC LEARNING FILE

=> fil reg



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

421 REFERENCES IN FILE CA (1907 TO DATE)
11 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
421 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L22 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2004 ACS on STN
RN 3380-34-5 REGISTRY
CN Phenol, 5-chloro-2-(2,4-dichlorophenoxy)- (7CI, 8CI, 9CI) (CA INDEX NAME)
OTHER NAMES:
CN 2',4',4-Trichloro-2-hydroxydiphenyl ether
CN 2',4,4'-Trichloro-2-hydroxydiphenyl ether
CN 2'-Hydroxy-2,4,4'-trichlorodiphenyl ether
CN 2,2'-Oxybis(1',5'-dichlorophenyl-5-chlorophenol)
CN 2,4,4'-Trichloro-2'-hydroxydiphenyl ether
CN 2-Hydroxy-2',4,4'-trichlorodiphenyl ether
CN 3-Chloro-6-(2,4-dichlorophenoxy)phenol
CN 4-Chloro-2-hydroxyphenyl 2,4-dichlorophenyl ether
CN 5-Chloro-2-(2,4-dichlorophenoxy)phenol
CN Aquasept
CN Bacti-Stat soap
CN Cansan TCH
CN CH 3565
CN CH 3635
CN DP 300
CN Gamophen
CN Irgacare MP
CN Irgacide LP 10
CN Irgaguard B 1000
CN Irgasan
CN Irgasan CH 3565
CN Irgasan DP 30
CN Irgasan DP 300
CN Irgasan DP 3000
CN Irgasan DP 400
CN Irgasan PE 30
CN Irgasan PG 60
CN Microban Additive B
CN Microban B
CN NM 100
CN Oletron
CN Sanitized XTX
CN Sapoderm
CN SterZac
CN TCCP
CN THDP
CN Tinosan AM 100
CN Tinosan AM 110
CN **Triclosan**
CN Ultra Fresh NM 100
CN Vinyzene DP 7000

```
FILE 'STNGUIDE' ENTERED AT 09:04:34 ON 13 DEC 2004
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AND TECHNOLOGY CORPORATION, AND FACHINFORMATIONSZENTRUM KARLSRUHE

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Dec 10, 2004 (20041210/UP).

=>

     FILE 'REGISTRY' ENTERED AT 09:03:54 ON 13 DEC 2004
L20             1 S TRICLOSAN/CN
L21             1 S CERULENIN/CN


=> s l20-l21
L22           2 (L20 OR L21)

=> => d ide 1-2

L22  ANSWER 1 OF 2  REGISTRY  COPYRIGHT 2004 ACS on STN
RN   17397-89-6  REGISTRY
CN   Oxiranecarboxamide, 3-[(4E,7E)-1-oxo-4,7-nonadienyl]-, (2R,3S)- (9CI)  (CA
     INDEX NAME)
OTHER CA INDEX NAMES:
CN   7,10-Dodecadienamide, 2,3-epoxy-4-oxo- (8CI)
CN   Oxiranecarboxamide, 3-(1-oxo-4,7-nonadienyl)-, [2R-
     [2α,3α(4E,7E)]]-
OTHER NAMES:
CN   (+)-Cerulenin
CN   Cerulenin
CN   Helicocerin
FS   STEREOSEARCH
DR   11052-24-7, 23557-85-9
MF   C12 H17 N O3
LC   STN Files:   ADISINSIGHT, ADISNEWS, AGRICOLA, BEILSTEIN*, BIOBUSINESS,
       BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CHEMCATS,
       CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, DDFU, DRUGU, EMBASE, MEDLINE,
       MRCK*, NAPRALERT, PROMT, RTECS*, TOXCENTER, USPAT2, USPATFULL
         (*File contains numerically searchable property data)
     Other Sources:   EINECS**
         (**Enter CHEMLIST File for up-to-date regulatory information)
DT.CA  CAplus document type:  Conference; Dissertation; Journal; Patent; Report
RL.P   Roles from patents:  ANST (Analytical study); BIOL (Biological study);
       PREP (Preparation); PROC (Process); RACT (Reactant or reagent); USES
       (Uses)
RLD.P  Roles for non-specific derivatives from patents:  BIOL (Biological
       study); PRP (Properties); USES (Uses)
RL.NP  Roles from non-patents:  ANST (Analytical study); BIOL (Biological
       study); FORM (Formation, nonpreparative); MSC (Miscellaneous); PREP
       (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or
       reagent); USES (Uses); NORL (No role in record)
RLD.NP Roles for non-specific derivatives from non-patents:  ANST (Analytical
       study); BIOL (Biological study); FORM (Formation, nonpreparative); PREP
       (Preparation); PRP (Properties); USES (Uses)

Absolute stereochemistry.
Double bond geometry as shown.
```

=> fil lreg

FILE 'LREGISTRY' ENTERED AT 09:04:26 ON 13 DEC 2004
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LREGISTRY IS A STATIC LEARNING FILE

=> fil reg

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provided by InfoChem.

STRUCTURE FILE UPDATES: 10 DEC 2004 HIGHEST RN 796738-17-5
DICTIONARY FILE UPDATES: 10 DEC 2004 HIGHEST RN 796738-17-5

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> fil hcap

FILE 'HCAPLUS' ENTERED AT 09:04:30 ON 13 DEC 2004
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FILE COVERS 1907 - 13 Dec 2004 VOL 141 ISS 25
FILE LAST UPDATED: 12 Dec 2004 (20041212/ED)

This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> file stnguide

```
>>> SMILES and ISOSMILES strings are no longer available as
    Derwent Chemistry Resource display fields  <<<

=> fil biotechds

FILE 'BIOTECHDS' ENTERED AT 13:34:36 ON 13 DEC 2004
COPYRIGHT (C) 2004 THE THOMSON CORPORATION

FILE LAST UPDATED: 8 DEC 2004        <20041208/UP>

>>> USE OF THIS FILE IS LIMITED TO BIOTECH SUBSCRIBERS <<<

>>> NEW CLASSIFICATION SYSTEM FROM 2002 ONWARDS - SEE HELP CLA <<<

>>> NEW DISPLAY FIELDS LS AND LS2 (LEGAL STATUS DATA FROM
    THE INPADOC DATABASE) AVAILABLE   -   SEE NEWS <<<

=> fil biotechno

FILE 'BIOTECHNO' ENTERED AT 13:34:43 ON 13 DEC 2004
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FILE LAST UPDATED: 7 JAN 2004        <20040107/UP>
FILE COVERS 1980 TO 2003.

>>>  BIOTECHNO IS NO LONGER BEING UPDATED AS OF 2004  <<<

>>>  SIMULTANEOUS LEFT AND RIGHT TRUNCATION AVAILABLE IN
     /CT AND BASIC INDEX  <<<

=> fil drugu

FILE 'DRUGU' ENTERED AT 13:34:47 ON 13 DEC 2004
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FILE LAST UPDATED: 8 DEC 2004        <20041208/UP>
>>>  DERWENT DRUG FILE (SUBSCRIBER)  <<<

>>>  FILE COVERS 1983 TO DATE  <<<
>>>  THESAURUS AVAILABLE IN /CT  <<<

>>>  A RECENT REVIEW OF PSYCHIATRIC DISEASE KEYWORDS USED
     IN DERWENT DRUG FILE HAS PROMPTED A REVISION BASED
     ON STANDARD TERMS USED IN DSM-IV (DIAGNOSTIC AND
     STATISTICAL MANUAL OF MENTAL DISORDERS - FOURTH
     EDITION).
     FOR FURTHER DETAILS:
http://thomsonderwent.com/derwenthome/support/userguides/lit_guide


=> file stnguide

FILE 'STNGUIDE' ENTERED AT 13:34:53 ON 13 DEC 2004
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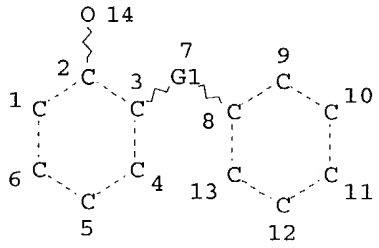
FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Dec 10, 2004 (20041210/UP).
```

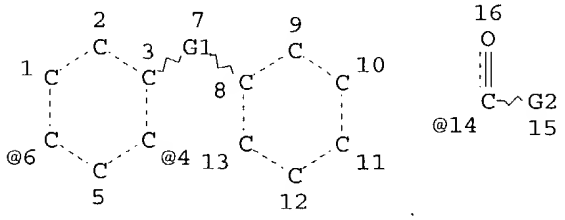
```
=> d que l163
L23           44 SEA FILE=REGISTRY ABB=ON  PLU=ON  3380-34-5/RN,CRN
L24            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  17397-89-6/RN,CRN
L39              SCR 2043 2052 2050
L40              SCR 1929
L42              STR
```




```
VAR G1=CH2/O/S
NODE ATTRIBUTES:
CONNECT IS E1  RC AT  14
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  14

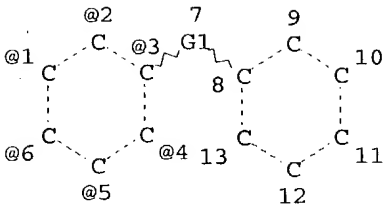
STEREO ATTRIBUTES: NONE
L44         4711 SEA FILE=REGISTRY SSS FUL ((L40 NOT L39) AND L42)
L46              STR
```




```
VAR G1=CH2/O/S
VAR G2=H/17
VPA 14-6/4 U
NODE ATTRIBUTES:
NSPEC   IS RC     AT  17
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  17

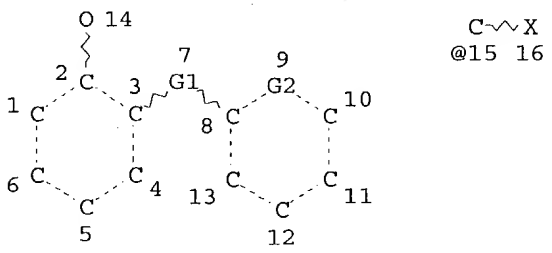
STEREO ATTRIBUTES: NONE
L48           19 SEA FILE=REGISTRY SUB=L44 SSS FUL L46
L49              STR
```



VAR G1=CH2/O/S
VPA 14-3/4/5/6/2/1 U
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 14

STEREO ATTRIBUTES: NONE
L51 8 SEA FILE=REGISTRY SUB=L48 SSS FUL L49
L52 STR



VAR G1=CH2/O/S
VAR G2=CH/15
NODE ATTRIBUTES:
CONNECT IS E1 RC AT 14
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

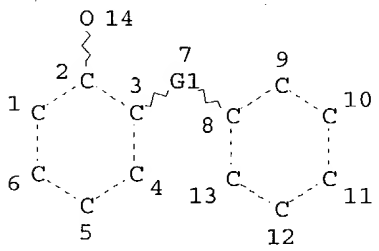
GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 16

STEREO ATTRIBUTES: NONE
L54 3 SEA FILE=REGISTRY SUB=L51 SSS FUL L52
L55 48 SEA FILE=REGISTRY ABB=ON PLU=ON L23 OR L24 OR L54
L59 17901 SEA FILE=HCAPLUS ABB=ON PLU=ON ANTIMALARIALS+PFT,NT,RT,RTCS/CT
L60 7661 SEA FILE=HCAPLUS ABB=ON PLU=ON MALARIA+PFT,NT/CT
L61 10542 SEA FILE=HCAPLUS ABB=ON PLU=ON "PLASMODIUM (MALARIAL GENUS)"+PFT,NT/CT
L62 1804 SEA FILE=HCAPLUS ABB=ON PLU=ON "PLASMODIUM BERGHEI"+PFT,NT/CT

L63 288 SEA FILE=HCAPLUS ABB=ON PLU=ON PLASMODIUM/CT
L64 215411 SEA FILE=HCAPLUS ABB=ON PLU=ON (FATTY ACID?)/OBI
L65 102974 SEA FILE=HCAPLUS ABB=ON PLU=ON "FATTY ACIDS, BIOLOGICAL STUDIES"+PFT,NT/CT

```
L66      348288 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "FATTY ACIDS"+PFT,NT/CT
L67           8 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "FATTY ACID?"/CW
L68        2534 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L55
L69          42 SEA FILE=HCAPLUS ABB=ON  PLU=ON  3380-34-5D?
L70         421 SEA FILE=HCAPLUS ABB=ON  PLU=ON  17397-89-6?
L71         417 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ((L59 OR L60 OR L61 OR L62 OR
                L63)) AND ((L64 OR L65 OR L66 OR L67))
L72          28 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L59 OR L60 OR L61 OR L62 OR
                L63) AND (L68 OR L69 OR L70)
L75       21136 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L64 OR L65 OR L66 OR L67)
                (L) (?SYNTH? OR ?PROPAGA? OR ?GENERAT? OR ?PERPETUAT?)
L77       22131 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L64 OR L65 OR L66 OR L67)
                (L)(?INHIBIT? OR ?TARGET? OR ?RUPT? OR ?BLOCK? OR ?STOP?)
L80        3768 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L75 (L) L77
L81          19 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L71 AND L80
L82          43 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L72 OR L81
L163         25 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L82 AND (AY<2002 OR PY<2002
                OR PRY<2002)

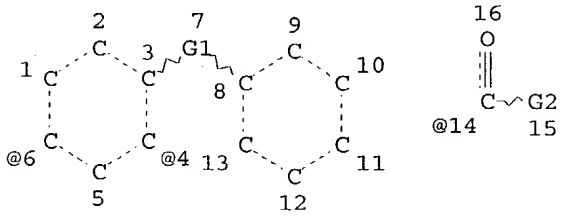

=> d que l164
L23          44 SEA FILE=REGISTRY ABB=ON  PLU=ON  3380-34-5/RN,CRN
L24           1 SEA FILE=REGISTRY ABB=ON  PLU=ON  17397-89-6/RN,CRN
L39             SCR 2043 2052 2050
L40             SCR 1929
L42             STR
```




```
VAR G1=CH2/O/S
NODE ATTRIBUTES:
CONNECT IS E1  RC AT  14
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  14

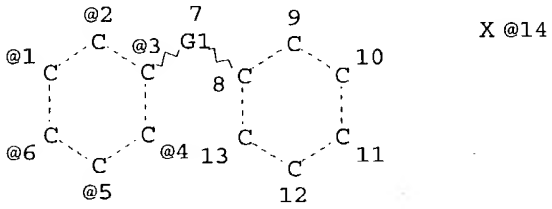
STEREO ATTRIBUTES: NONE
L44        4711 SEA FILE=REGISTRY SSS FUL ((L40 NOT L39) AND L42)
L46             STR
```



VAR G1=CH2/O/S
VAR G2=H/17
VPA 14-6/4 U
NODE ATTRIBUTES:
NSPEC IS RC AT 17
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 17

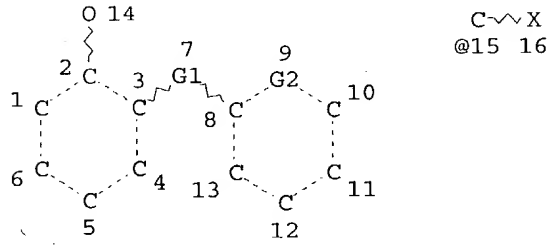
STEREO ATTRIBUTES: NONE
L48 19 SEA FILE=REGISTRY SUB=L44 SSS FUL L46
L49 STR



VAR G1=CH2/O/S
VPA 14-3/4/5/6/2/1 U
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 14

STEREO ATTRIBUTES: NONE
L51 8 SEA FILE=REGISTRY SUB=L48 SSS FUL L49
L52 STR

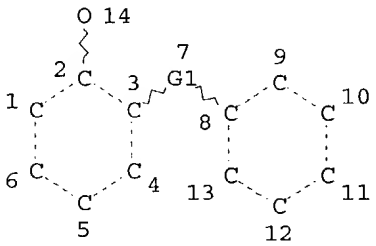


VAR G1=CH2/O/S
VAR G2=CH/15
NODE ATTRIBUTES:
CONNECT IS E1 RC AT 14
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 16

```
STEREO ATTRIBUTES: NONE
L54             3 SEA FILE=REGISTRY SUB=L51 SSS FUL L52
L55            48 SEA FILE=REGISTRY ABB=ON  PLU=ON  L23 OR L24 OR L54
L85         27615 SEA FILE=MEDLINE ABB=ON  PLU=ON  MALARIA+PFT,NT/CT
L86         20347 SEA FILE=MEDLINE ABB=ON  PLU=ON  "PLASMODIUM INFECTIONS"/CT
L87         20347 SEA FILE=MEDLINE ABB=ON  PLU=ON  "INFECTIONS, PLASMODIUM"/CT
L88             0 SEA FILE=MEDLINE ABB=ON  PLU=ON  PALUDISM/CT
L89         43717 SEA FILE=MEDLINE ABB=ON  PLU=ON  ANTIMALARIALS+PFT,NT/CT
L90          9197 SEA FILE=MEDLINE ABB=ON  PLU=ON  "ANTI-MALARIALS"/CT
L91          9197 SEA FILE=MEDLINE ABB=ON  PLU=ON  "ANTIMALARIAL AGENTS"/CT
L92          9197 SEA FILE=MEDLINE ABB=ON  PLU=ON  "ANTIMALARIAL DRUGS"/CT
L93        117404 SEA FILE=MEDLINE ABB=ON  PLU=ON  ?FATTY? (2A) ?ACID?
L94       1500111 SEA FILE=MEDLINE ABB=ON  PLU=ON  (?SYNTH? OR ?PROPAGA? OR
                  ?GENERAT? OR ?PERPETUAT?)
L95       2237461 SEA FILE=MEDLINE ABB=ON  PLU=ON  (?INHIBIT? OR ?TARGET? OR
                  ?RUPT? OR ?BLOCK? OR ?STOP?)
L96        348606 SEA FILE=MEDLINE ABB=ON  PLU=ON  L94 (L) L95
L97          6512 SEA FILE=MEDLINE ABB=ON  PLU=ON  L93 (L) L96
L98            43 SEA FILE=MEDLINE ABB=ON  PLU=ON  (L85 OR L86 OR L87 OR L88 OR
                  L89 OR L90 OR L91 OR L92) AND L97
L99               SEL PLU=ON L55 1- CHEM :    111 TERMS
L100         1541 SEA FILE=MEDLINE ABB=ON  PLU=ON  L99
L101           19 SEA FILE=MEDLINE ABB=ON  PLU=ON  L100 AND (L85 OR L86 OR L87
                  OR L88 OR L89 OR L90 OR L91 OR L92)
L130           15 SEA FILE=MEDLINE ABB=ON  PLU=ON  L98 AND ?MALARI?
L131           28 SEA FILE=MEDLINE ABB=ON  PLU=ON  L101 OR L130
L164           18 SEA FILE=MEDLINE ABB=ON  PLU=ON  L131 AND PY<2002


=> d que l165
L23            44 SEA FILE=REGISTRY ABB=ON  PLU=ON  3380-34-5/RN,CRN
L24             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  17397-89-6/RN,CRN
L39               SCR 2043 2052 2050
L40               SCR 1929
L42               STR
```




```
VAR G1=CH2/O/S
NODE ATTRIBUTES:
CONNECT IS E1  RC AT  14
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  14

STEREO ATTRIBUTES: NONE
L44          4711 SEA FILE=REGISTRY SSS FUL ((L40 NOT L39) AND L42)
L46               STR
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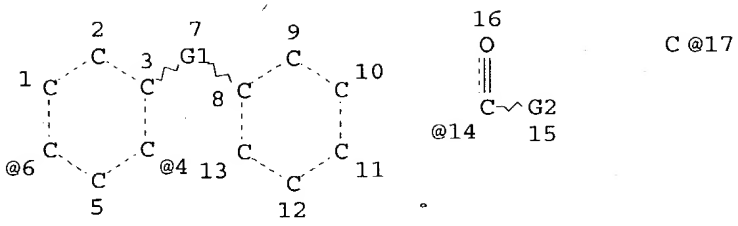
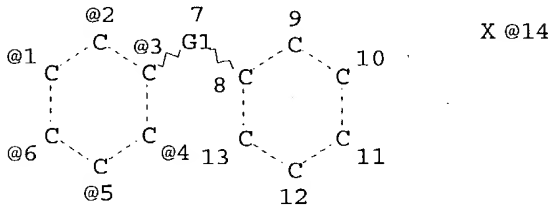


VAR G1=CH2/O/S
VAR G2=H/17
VPA 14-6/4 U
NODE ATTRIBUTES:
NSPEC IS RC AT 17
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 17

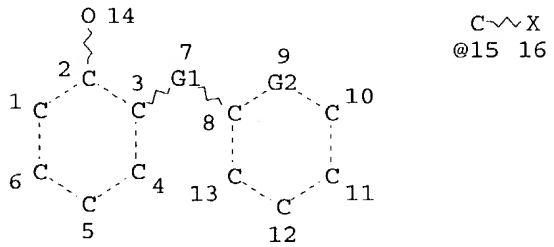
STEREO ATTRIBUTES: NONE
L48 19 SEA FILE=REGISTRY SUB=L44 SSS FUL L46
L49 STR



VAR G1=CH2/O/S
VPA 14-3/4/5/6/2/1 U
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 14

STEREO ATTRIBUTES: NONE
L51 8 SEA FILE=REGISTRY SUB=L48 SSS FUL L49
L52 STR



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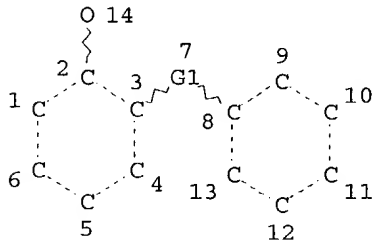
VAR G1=CH2/O/S
VAR G2=CH/15
NODE ATTRIBUTES:
CONNECT IS E1  RC AT  14
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  16

STEREO ATTRIBUTES: NONE
L54            3 SEA FILE=REGISTRY SUB=L51 SSS FUL L52
L55           48 SEA FILE=REGISTRY ABB=ON  PLU=ON  L23 OR L24 OR L54
L108       86507 SEA FILE=EMBASE ABB=ON  PLU=ON  ?FATTY? (2A) ?ACID?
L109     1205905 SEA FILE=EMBASE ABB=ON  PLU=ON  (?SYNTH? OR ?PROPAGA? OR
                 ?GENERAT? OR ?PERPETUAT?)
L110     2120275 SEA FILE=EMBASE ABB=ON  PLU=ON  (?INHIBIT? OR ?TARGET? OR
                 ?ANTAGON? OR ?RUPT? OR ?BLOCK? OR ?STOP?)
L113       20977 SEA FILE=EMBASE ABB=ON  PLU=ON  MALARIA+NT/CT
L114        2136 SEA FILE=EMBASE ABB=ON  PLU=ON  "PLASMODIUM BERGHEI"/CT
L115       12978 SEA FILE=EMBASE ABB=ON  PLU=ON  "PLASMODIUM FALCIPARUM"/CT
L116       39837 SEA FILE=EMBASE ABB=ON  PLU=ON  "ANTIMALARIAL AGENT"+PFT,NT/CT

L117               SEL  PLU=ON  L55 1- CHEM :     111 TERMS
L118        1685 SEA FILE=EMBASE ABB=ON  PLU=ON  L117
L121        1250 SEA FILE=EMBASE ABB=ON  PLU=ON  L108 (15A) (L109 (7A) L110)
L122          22 SEA FILE=EMBASE ABB=ON  PLU=ON  (L113 OR L114 OR L115 OR L116)
                 AND L121
L123          52 SEA FILE=EMBASE ABB=ON  PLU=ON  (L113 OR L114 OR L115 OR L116)
                 AND L118
L124          65 SEA FILE=EMBASE ABB=ON  PLU=ON  (L122 OR L123)
L128          37 SEA FILE=EMBASE ABB=ON  PLU=ON  L124 AND ?MALARI?
L165          13 SEA FILE=EMBASE ABB=ON  PLU=ON  L128 AND PY<2002


=> d que l166
L23           44 SEA FILE=REGISTRY ABB=ON  PLU=ON  3380-34-5/RN,CRN
L24            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  17397-89-6/RN,CRN
L39              SCR 2043 2052 2050
L40              SCR 1929
L42              STR
```

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VAR G1=CH2/O/S
NODE ATTRIBUTES:
CONNECT IS E1  RC AT  14
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
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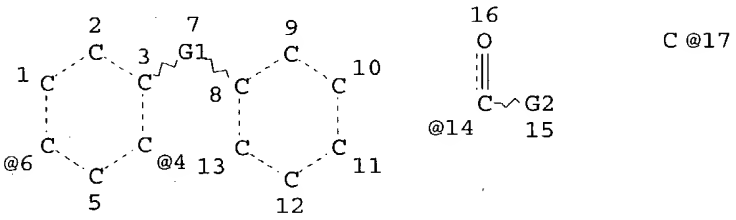
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 14

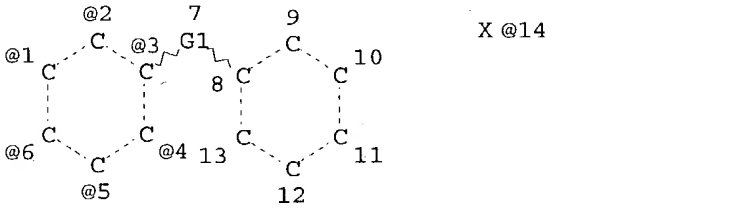
STEREO ATTRIBUTES: NONE
L44 4711 SEA FILE=REGISTRY SSS FUL ((L40 NOT L39) AND L42)
L46 STR



VAR G1=CH2/O/S
VAR G2=H/17
VPA 14-6/4 U
NODE ATTRIBUTES:
NSPEC IS RC AT 17
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 17

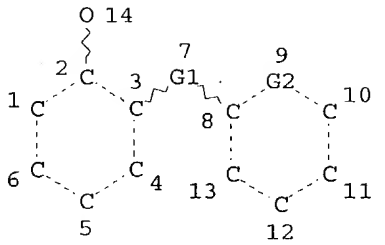
STEREO ATTRIBUTES: NONE
L48 19 SEA FILE=REGISTRY SUB=L44 SSS FUL L46
L49 STR



VAR G1=CH2/O/S
VPA 14-3/4/5/6/2/1 U
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 14

STEREO ATTRIBUTES: NONE
L51 8 SEA FILE=REGISTRY SUB=L48 SSS FUL L49
L52 STR




```
VAR G1=CH2/O/S
VAR G2=CH/15
NODE ATTRIBUTES:
CONNECT IS E1  RC AT  14
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  16

STEREO ATTRIBUTES: NONE
L54            3 SEA FILE=REGISTRY SUB=L51 SSS FUL L52
L55           48 SEA FILE=REGISTRY ABB=ON  PLU=ON  L23 OR L24 OR L54
L133      136663 SEA FILE=BIOSIS ABB=ON  PLU=ON  ?FATTY? (2A) ?ACID?
L134     1545074 SEA FILE=BIOSIS ABB=ON  PLU=ON  (?SYNTH? OR ?PROPAGA? OR
                 ?GENERAT? OR ?PERPETUAT?)
L135     2397099 SEA FILE=BIOSIS ABB=ON  PLU=ON  (?INHIBIT? OR ?TARGET? OR
                 ?MODULAT? OR ?MODERAT? OR ?ANTAGON? OR ?RUPT? OR ?BLOCK? OR
                 ?STOP?)
L136         8131 SEA FILE=BIOSIS ABB=ON  PLU=ON  L133 (L) L134 (L) L135
L138        31383 SEA FILE=BIOSIS ABB=ON  PLU=ON  ?MALARI?
L140           36 SEA FILE=BIOSIS ABB=ON  PLU=ON  L138 (L) L136
L141              SEL  PLU=ON L55 1- CHEM :      111 TERMS
L142         1809 SEA FILE=BIOSIS ABB=ON  PLU=ON  L141
L143           21 SEA FILE=BIOSIS ABB=ON  PLU=ON  L142 AND L138
L145           16 SEA FILE=BIOSIS ABB=ON  PLU=ON  L142 (L) L138
L146           21 SEA FILE=BIOSIS ABB=ON  PLU=ON  L143 OR L145
L150           45 SEA FILE=BIOSIS ABB=ON  PLU=ON  L146 OR L140
L166           17 SEA FILE=BIOSIS ABB=ON  PLU=ON  L150 AND (PY<2002 OR MY<2002)


=> d que l161
L149       74200 SEA FILE=WPIX ABB=ON  PLU=ON  (?FATTY? (2A) ?ACID?)/BIX
L151       95642 SEA FILE=WPIX ABB=ON  PLU=ON  ((?SYNTH? OR ?PROPAGA? OR
                 ?GENERAT? OR ?PERPETUAT?) (7A) (?INHIBIT? OR ?TARGET? OR
                 ?MODULAT? OR ?MODERAT? OR ?ANTAGON? OR ?RUPT? OR ?BLOCK? OR
                 ?STOP?))/BIX
L152         220 SEA FILE=WPIX ABB=ON  PLU=ON  L149 (7A) L151
L153         434 SEA FILE=WPIX ABB=ON  PLU=ON  A61P033-06/IPC
L154        2183 SEA FILE=WPIX ABB=ON  PLU=ON  (B14-A03B OR B12-B03 OR C14-A03B
                 OR C12-B03)/MC
L159         743 SEA FILE=WPIX ABB=ON  PLU=ON  ?TRICLOSAN?/BIX
L160          58 SEA FILE=WPIX ABB=ON  PLU=ON  ?CERULENIN?/BIX
L161           5 SEA FILE=WPIX ABB=ON  PLU=ON  (L153 OR L154) AND (L152 OR L159
                 OR L160)
```

```
=> d his l175

     (FILE 'BIOTECHDS, BIOTECHNO, DRUGU' ENTERED AT 13:25:19 ON 13 DEC 2004)
L175          21 DUP REM L174 (6 DUPLICATES REMOVED)

=> d que l175
L167       11938 SEA ?MALARI?
L168        4570 SEA ANTIMALARI?
L169       13963 SEA (L167 OR L168)
L170       94802 SEA (?SYNTH? OR ?PROPAGA? OR ?GENERAT? OR ?PERPETUAT?) (7A)
                 (?INHIBIT? OR ?TARGET? OR ?MODULAT? OR ?MODERAT? OR ?ANTAGON?
                 OR ?RUPT? OR ?BLOCK? OR ?STOP?)
L171         660 SEA (?FATTY? (2A) ?ACID?) (7A) L170
L172         749 SEA ?TRICLOSAN? OR ?CERULENIN?
L174          27 SEA L169 (L)(L171 OR L172)
L175          21 DUP REM L174 (6 DUPLICATES REMOVED)


=> dup rem l163 l164 l166 l165 l161 l175

FILE 'HCAPLUS' ENTERED AT 13:36:14 ON 13 DEC 2004
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PROCESSING COMPLETED FOR L164
PROCESSING COMPLETED FOR L166
PROCESSING COMPLETED FOR L165
PROCESSING COMPLETED FOR L161
PROCESSING COMPLETED FOR L175
L181          71 DUP REM L163 L164 L166 L165 L161 L175 (28 DUPLICATES REMOVED)
                 ANSWERS '1-25' FROM FILE HCAPLUS
                 ANSWERS '26-40' FROM FILE MEDLINE
                 ANSWERS '41-51' FROM FILE BIOSIS
                 ANSWERS '52-56' FROM FILE EMBASE
                 ANSWERS '57-58' FROM FILE WPIX
                 ANSWER '59' FROM FILE BIOTECHDS
                 ANSWERS '60-67' FROM FILE BIOTECHNO
                 ANSWERS '68-71' FROM FILE DRUGU
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=> file stnguide

FILE 'STNGUIDE' ENTERED AT 13:36:53 ON 13 DEC 2004
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AND TECHNOLOGY CORPORATION, AND FACHINFORMATIONSZENTRUM KARLSRUHE

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Dec 10, 2004 (20041210/UP).

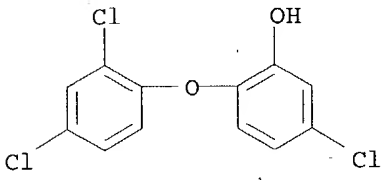
=> d ibib abs ed hitstr hitind
YOU HAVE REQUESTED DATA FROM FILE 'WPIX, HCAPLUS, MEDLINE, EMBASE, BIOSIS,
BIOTECHDS, BIOTECHNO, DRUGU' - CONTINUE? (Y)/N:y


L181 ANSWER 1 OF 71  HCAPLUS  COPYRIGHT 2004 ACS on STN DUPLICATE 1
ACCESSION NUMBER:          2003:242144  HCAPLUS
DOCUMENT NUMBER:           138:243344
TITLE:                     Triclosan dosage forms for malaria treatment
INVENTOR(S):               Loetter, Antonie Philippus; Du Preez, Jan Lourens;
                           Collins, Lindi-May
PATENT ASSIGNEE(S):        Potchefstroom University for Christian Higher
                           Education, S. Afr.
SOURCE:                    PCT Int. Appl., 32 pp.
                           CODEN: PIXXD2
DOCUMENT TYPE:             Patent
LANGUAGE:                  English
FAMILY ACC. NUM. COUNT:    1
PATENT INFORMATION:

     PATENT NO.             KIND   DATE        APPLICATION NO.          DATE
     ---------------        ----   --------    ---------------------    --------
     WO 2003024421           A2    20030327    WO 2002-ZA145            20020918 <--
     WO 2003024421           A3    20040122
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
             FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF,
             CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     EP 1427400              A2    20040616    EP 2002-766552           20020918 <--
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK
     BR 2002012605           A     20040817    BR 2002-12605            20020918 <--
PRIORITY APPLN. INFO.:                         ZA 2001-7414         A   20010918 <--
                                               WO 2002-ZA145        W   20020918

AB   This invention relates to a dosage form of triclosan for use in the
     treatment of malaria.  This invention further relates to use of a
     triclosan emulsion or oil solution in the preparation of a composition for use
in the
     treatment, including prophylaxis, of malaria.  A method of measuring
     plasma levels of triclosan is also disclosed.  Thus, an emulsion contained
     triclosan 16, sunflower oil 34, BHA 0.01, Span-80 5, Tween-80 5,
     methylparaben 0.1, propylparaben 0.02, saccharin sodium 0.1, and water qs
     to 100 g.
```

ED Entered STN: 28 Mar 2003
IT **3380-34-5**, Triclosan
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(triclosan dosage forms for malaria treatment)
RN 3380-34-5 HCAPLUS
CN Phenol, 5-chloro-2-(2,4-dichlorophenoxy)- (7CI, 8CI, 9CI) (CA INDEX NAME)



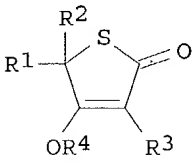
IC ICM A61K009-00
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1
IT **Antimalarials**
Antioxidants
Drug bioavailability
Emulsifying agents
Human
Malaria
Preservatives
Surfactants
Sweetening agents
(triclosan dosage forms for malaria treatment)
IT **3380-34-5**, Triclosan
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(triclosan dosage forms for malaria treatment)

=> d ibib abs ed hitstr hitind 2-25
YOU HAVE REQUESTED DATA FROM FILE 'WPIX, HCAPLUS, MEDLINE, EMBASE, BIOSIS, BIOTECHDS, BIOTECHNO, DRUGU' - CONTINUE? (Y)/N:y

L181 ANSWER 2 OF 71 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 2001:507522 HCAPLUS
DOCUMENT NUMBER: 135:87153
TITLE: Thiolactomycin analogs and compositions for use in **inhibiting** endoparasitic **fatty acid biosynthesis**
INVENTOR(S): Berry, Colin; Harwood, John L.
PATENT ASSIGNEE(S): University College Cardiff Consultants Limited, UK
SOURCE: PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001049278	A2	20010712	WO 2001-GB82	20010108 <--

WO 2001049278 A3 20020411
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
CA 2396234 AA 20010712 CA 2001-2396234 20010108 <--
EP 1244436 A2 20021002 EP 2001-900204 20010108 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
JP 2003519177 T2 20030617 JP 2001-549646 20010108 <--
US 2003171420 A1 20030911 US 2002-169601 20021120 <--
PRIORITY APPLN. INFO.: GB 2000-131 A 20000106 <--
WO 2001-GB82 W 20010108 <--
OTHER SOURCE(S): MARPAT 135:87153
GI



I

AB The invention discloses the use of at least one compound I [R1 = H, alkyl, (cyano)alkylene, alkenyl, alkynyl, etc.; R2, R3 = alkyl, cycloalkyl; R4 = H, alkyl; including racemic mixts. and enantiomers of compound when latter is chiral, but excluding racemic mixture of chiral compound where R1 = CH2=CH-C(CH3)=CH-, R2, R3 = Me, and R4 = H], or a pharmaceutically acceptable salt or prodrug thereof, as an inhibitor of at least one β-ketoacyl acyl carrier protein synthase operable in the fatty acid biosynthesis of endoparasites.

ED Entered STN: 13 Jul 2001
IC ICM A61K031-00
CC 1-5 (Pharmacology)
Section cross-reference(s): 63
ST endoparasite **fatty acid biosynthesis** **inhibitor** thiolactomycin deriv; ketoacyl ACP **synthase** **inhibitor** endoparasite thiolactomycin deriv
IT Parasite
(endo-; thiolactomycin analogs and compns. for use in **inhibiting** endoparasitic **fatty acid biosynthesis**)
IT Drug delivery systems
(prodrugs; thiolactomycin analogs and compns. for use in **inhibiting** endoparasitic **fatty acid biosynthesis**)
IT **Antimalarials**
Apicomplexa
Drug delivery systems
Eimeria
Eimeria tenella
Parasiticides

Plasmodium (malarial genus)
Plasmodium falciparum
(thiolactomycin analogs and compns. for use in **inhibiting** endoparasitic **fatty acid biosynthesis**)

IT **Fatty acids, biological studies**
RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(thiolactomycin analogs and compns. for use in **inhibiting** endoparasitic **fatty acid biosynthesis**)

IT 99265-28-8
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(thiolactomycin analogs and compns. for use in **inhibiting** endoparasitic **fatty acid biosynthesis**)

IT 82079-32-1D, Thiolactomycin, analogs 96843-12-8 157772-22-0
157772-23-1 157772-24-2 157772-25-3 157772-26-4 157772-27-5
348113-79-1 348113-80-4 348113-81-5 348113-82-6 348113-83-7
348113-84-8 348113-85-9 348113-86-0 348113-87-1 348113-88-2
348113-89-3 348113-90-6
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(thiolactomycin analogs and compns. for use in **inhibiting** endoparasitic **fatty acid biosynthesis**)

IT 9077-10-5, β-Ketoacyl acyl carrier protein **synthase**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(thiolactomycin analogs and compns. for use in **inhibiting** endoparasitic **fatty acid biosynthesis**)

L181 ANSWER 3 OF 71 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 4
ACCESSION NUMBER: 2001:12206 HCAPLUS
DOCUMENT NUMBER: 134:66128
TITLE: Use of hydroxydiphenyl ether class of chemicals, as exemplified by triclosan, as an antimalarial and identification of **fatty acid synthesis** as its **target**
INVENTOR(S): Namita, Surolina; Dharmarajan, Kamalapriya; Nagaraja, Thirumalapura Ramadhani
PATENT ASSIGNEE(S): Jawaharlal Nehru Centre for Advanced Scientific Research, India
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

App

PATENT NO.	KIND	DATE		DATE
WO 2001000138	A2	20010104		19990623 <--
WO 2001000138	A3	20020711		
WO 2001000138	B1	20021017		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,

ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9954424	A1	20010131	AU 1999-54424	19990623 <--
BR 9913324	A	20010731	BR 1999-13324	19990623 <--
EP 1137386	A2	20011004	EP 1999-940451	19990623 <--

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

PRIORITY APPLN. INFO.: WO 1999-IN26 A 19990623 <--

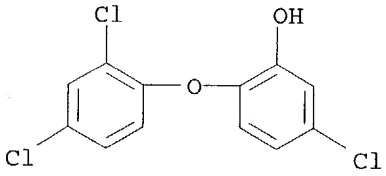
AB The use of hydroxydiphenyl ether class of chems., as exemplified by triclosan, (2,4,4'-trichloro-2'-hydroxydiphenyl ether), for both treatment and design of therapeutics for treatment of malaria is reported. More specifically, the present invention relates to identification of fatty acid synthesis as target for this compound as well as a key enzyme involved in synthesizing them. Inhibitory effects of triclosan on the growth of Plasmodium falciparum is shown. Mice infected with P. berghei were injected with 8., 14.0, and 28.0 mg triclosan/kg were survived while all the control group died by day 9 of infection.

ED Entered STN: 05 Jan 2001

IT **3380-34-5**, Triclosan
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of hydroxydiphenyl ether class of chems. as antimalarial and identification of **fatty acid synthesis** as its **target**)

RN 3380-34-5 HCAPLUS

CN Phenol, 5-chloro-2-(2,4-dichlorophenoxy)- (7CI, 8CI, 9CI) (CA INDEX NAME)



IC ICM A61K

CC 1-5 (Pharmacology)
Section cross-reference(s): 61

ST hydroxydiphenyl ether antimalarial **fatty acid** synthesis; triclosan antimalarial **fatty acid** synthesis

IT Drug delivery systems
(injections, i.m.; use of hydroxydiphenyl ether class of chems. as antimalarial and identification of **fatty acid synthesis** as its **target**)

IT Drug delivery systems
(injections, i.p.; use of hydroxydiphenyl ether class of chems. as antimalarial and identification of **fatty acid synthesis** as its **target**)

IT **Antimalarials**
Plasmodium berghei
Plasmodium falciparum
(use of hydroxydiphenyl ether class of chems. as antimalarial and identification of **fatty acid synthesis** as its **target**)

IT **Fatty acids, biological studies**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(use of hydroxydiphenyl ether class of chems. as antimalarial and identification of **fatty acid synthesis** as

its **target**)

IT 101-84-8D, Diphenyl ether, hydroxy derivs. **3380-34-5**, Triclosan
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of hydroxydiphenyl ether class of chems. as antimalarial and identification of **fatty acid synthesis** as its **target**)

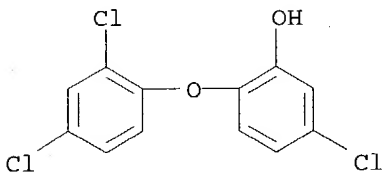
L181 ANSWER 4 OF 71 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 5
ACCESSION NUMBER: 2001:881182 HCAPLUS
DOCUMENT NUMBER: 136:130677
TITLE: Kinetic Determinants of the Interaction of Enoyl-ACP Reductase from Plasmodium falciparum with Its Substrates and Inhibitors
AUTHOR(S): Kapoor, Mili; Jamal Dar, M.; Surolia, Avadhesha; Surolia, Namita
CORPORATE SOURCE: Molecular Biophysics Unit, Indian Institute of Science, Bangalore, India
SOURCE: Biochemical and Biophysical Research Communications (**2001**), 289(4), 832-837
CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We have recently demonstrated that Plasmodium falciparum, unlike its human host, has the type II fatty acid synthase, in which steps of fatty acid biosynthesis are catalyzed by independent enzymes. This difference could be successfully exploited in the design of drugs specifically targeted at the different enzymes of this pathway in P. falciparum, without affecting the corresponding enzymes in humans. The importance of enoyl-ACP reductase (FabI) in the fatty acid biosynthesis pathway makes it an important target in antimalarial therapy. We report here the initial characterization of Plasmodium FabI expressed in Escherichia coli. The Km values of the enzyme for crotonyl-CoA and NADH were derived as 165 and 33 μM, resp. Triclosan shows competitive kinetics with respect to NADH but is uncompetitive with respect to NAD+, which shows that the binding of triclosan to the enzyme is facilitated in the presence of NAD+. (c) 2001 Academic Press.

ED Entered STN: 07 Dec 2001

IT **3380-34-5**, Triclosan
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(kinetic determinants of interaction of enoyl-ACP reductase from Plasmodium falciparum with substrates and inhibitors)

RN 3380-34-5 HCAPLUS
CN Phenol, 5-chloro-2-(2,4-dichlorophenoxy)- (7CI, 8CI, 9CI) (CA INDEX NAME)



CC 7-4 (Enzymes)

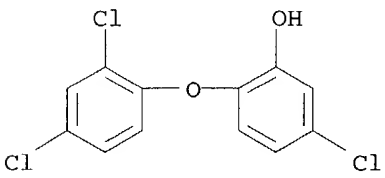
IT **Plasmodium falciparum**
(kinetic determinants of interaction of enoyl-ACP reductase from Plasmodium falciparum with substrates and inhibitors)

IT 53-84-9, NAD+ 58-68-4, NADH 992-67-6, Crotonyl-CoA **3380-34-5**, Triclosan 15764-52-0, 2,2'-Dihydroxydiphenyl ether 37251-08-4, Enoyl-ACP Reductase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(kinetic determinants of interaction of enoyl-ACP reductase from Plasmodium falciparum with substrates and inhibitors)
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L181 ANSWER 5 OF 71 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 8
ACCESSION NUMBER: 2001:295280 HCAPLUS
DOCUMENT NUMBER: 135:146842
TITLE: Structural Basis for Triclosan and NAD Binding to Enoyl-ACP Reductase of Plasmodium falciparum
AUTHOR(S): Suguna, Kaza; Surolia, Avadhesha; Surolia, Namita
CORPORATE SOURCE: Molecular Biophysics Unit, Indian Institute of Science, Bangalore, 560 012, India
SOURCE: Biochemical and Biophysical Research Communications (**2001**), 283(1), 224-228
CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Recent discovery of type II fatty acid synthase in the malarial parasite Plasmodium falciparum responsible for the most debilitating form of the disease in humans makes it ideal as a target for the development of novel antimalarials. Also, the identification of the enoyl-acyl carrier protein reductase from P. falciparum and the demonstration of its inhibition by triclosan [5-chloro-2-(2,4-dichlorophenoxy)phenol], a potent antibacterial compound, provide strong support for the above. In the studies reported here, a model of the enzyme in complex with triclosan and the cofactor NAD has been built by homol. modeling with a view to understand its binding properties and to explore the potential of triclosan as a lead compound in designing effective antimalarial drugs. The model indeed provided the structural rationale for its interaction with ligands and the cofactor and revealed unique characteristics of its binding site which could be exploited for improving the specificity of the inhibitors. (c) 2001 Academic Press.

ED Entered STN: 26 Apr 2001
IT **3380-34-5**, Triclosan
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(structural basis for triclosan and NAD binding to enoyl-ACP reductase of Plasmodium falciparum)
RN 3380-34-5 HCAPLUS
CN Phenol, 5-chloro-2-(2,4-dichlorophenoxy)- (7CI, 8CI, 9CI) (CA INDEX NAME)



CC 1-5 (Pharmacology)
IT **Antimalarials**
Molecular modeling

Plasmodium falciparum
(structural basis for triclosan and NAD binding to enoyl-ACP reductase of Plasmodium falciparum)

IT **3380-34-5**, Triclosan
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(structural basis for triclosan and NAD binding to enoyl-ACP reductase of Plasmodium falciparum)

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

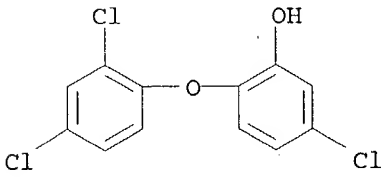
L181 ANSWER 6 OF 71 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 9
ACCESSION NUMBER: 2001:108315 HCAPLUS
DOCUMENT NUMBER: 134:290011
TITLE: Triclosan offers protection against blood stages of malaria by inhibiting enol-ACP reductase of Plasmodium falciparum
AUTHOR(S): Surolia, Namita; Surolia, Avadhesha
CORPORATE SOURCE: Molecular Biology and Genetics Unit, Jawaharlat Nehru Centre for Advanced Scientific Research, Jakkur, Bangalore, India
SOURCE: Nature Medicine (New York) (**2001**), 7(2), 167-173
CODEN: NAMEFI; ISSN: 1078-8956
PUBLISHER: Nature America Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The antimicrobial biocide triclosan [5-chloro-2-(2,4-dichlorophenoxy)phenol] potentially inhibits the growth of Plasmodium falciparum in vitro and, in a mouse model, Plasmodium berghei in vivo. Inhibition of [14C]acetate and [14C]malonyl-CoA incorporation into fatty acids in vivo and in vitro, resp., by triclosan implicate FabI as its target. Here we demonstrate that the enoyl-ACP reductase purified from p. falciparum is triclosan sensitive. Also, we present the evidence for the existence of FabI gene in p. falciparum. We establish the existence of the de novo fatty acid biosynthetic pathway in this parasite, and identify a key enzyme of this pathway for the development of new antimalarials.

ED Entered STN: 14 Feb 2001

IT **3380-34-5**, Triclosan
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(triclosan protects against blood stages of malaria by inhibiting enol-ACP reductase of Plasmodium falciparum)

RN 3380-34-5 HCAPLUS
CN Phenol, 5-chloro-2-(2,4-dichlorophenoxy)- (7CI, 8CI, 9CI) (CA INDEX NAME)



CC 1-5 (Pharmacology)
Section cross-reference(s): 10

IT **Fatty acids, biological studies**

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**synthesis**; triclosan protects against blood stages of malaria by **inhibiting** enol-ACP reductase of Plasmodium falciparum)

IT **Antimalarials**
Plasmodium (malarial genus)
(triclosan protects against blood stages of malaria by inhibiting enol-ACP reductase of Plasmodium falciparum)

IT **3380-34-5**, Triclosan
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(triclosan protects against blood stages of malaria by inhibiting enol-ACP reductase of Plasmodium falciparum)

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L181 ANSWER 7 OF 71 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 10
ACCESSION NUMBER: 2001:163531 HCAPLUS
DOCUMENT NUMBER: 135:16614
TITLE: Triclosan inhibits the growth of Plasmodium falciparum and Toxoplasma gondii by inhibition of Apicomplexan Fab I
AUTHOR(S): McLeod, R.; Muench, S. P.; Rafferty, J. B.; Kyle, D. E.; Mui, E. J.; Kirisits, M. J.; Mack, D. G.; Roberts, C. W.; Samuel, B. U.; Lyons, R. E.; Dorris, M.; Milhous, W. K.; Rice, D. W.
CORPORATE SOURCE: Department of Ophthalmology and Visual Sciences, The University of Chicago, 60637, Chicago, IL, USA
SOURCE: International Journal for Parasitology (**2001**), 31(2), 109-113
CODEN: IJPYBT; ISSN: 0020-7519
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

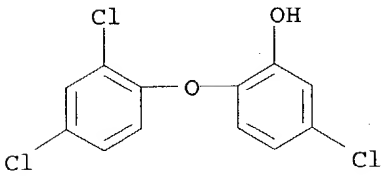
AB Fab I, enoyl acyl carrier protein reductase (ENR), is an enzyme used in fatty acid synthesis. It is a single chain polypeptide in plants, bacteria, and mycobacteria, but is part of a complex polypeptide in animals and fungi. Certain other enzymes in fatty acid synthesis in apicomplexan parasites appear to have multiple forms, homologous to either a plastid, plant-like single chain enzyme or more like the animal complex polypeptide chain. We identified a plant-like Fab I in Plasmodium falciparum and modelled the structure on the Brassica napus and Escherichia coli structures, alone and complexed to triclosan (5-chloro-2-[2,4 dichlorophenoxy] phenol), which confirmed all the requisite features of an ENR and its interactions with triclosan. Like the remarkable effect of triclosan on a wide variety of bacteria, this compound markedly inhibits growth and survival of the apicomplexan parasites P. falciparum and Toxoplasma gondii at low (i.e. IC50 .simeq. 150-2000 and 62 ng/mL, resp.) concns. Discovery and characterization of an apicomplexan Fab I and discovery of triclosan as lead compound provide means to rationally design novel inhibitory compds.

ED Entered STN: 08 Mar 2001

IT **3380-34-5**, Triclosan
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(triclosan inhibits growth of Plasmodium falciparum and Toxoplasma gondii by inhibition of Apicomplexan Fab I)

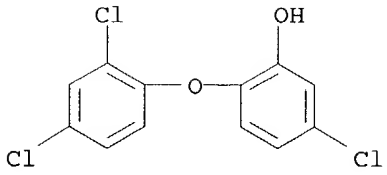
RN 3380-34-5 HCAPLUS

CN Phenol, 5-chloro-2-(2,4-dichlorophenoxy)- (7CI, 8CI, 9CI) (CA INDEX NAME)



CC 10-5 (Microbial, Algal, and Fungal Biochemistry)
IT Apicomplexa
Conformation
Plasmodium falciparum
Protein sequences
Toxoplasma gondii
(triclosan inhibits growth of Plasmodium falciparum and Toxoplasma gondii by inhibition of Apicomplexan Fab I)
IT **3380-34-5**, Triclosan
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(triclosan inhibits growth of Plasmodium falciparum and Toxoplasma gondii by inhibition of Apicomplexan Fab I)
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

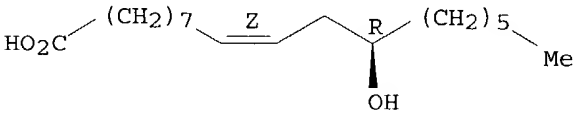
L181 ANSWER 8 OF 71 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 11
ACCESSION NUMBER: 2001:522092 HCAPLUS
DOCUMENT NUMBER: 135:298011
TITLE: Triclosan against malaria
AUTHOR(S): Kaiser, Annette; Gottwald, Andrea; Wiersch, Carolin
CORPORATE SOURCE: Institut fur Medizinische Parasitologie, Bonn, 53115, Germany
SOURCE: Deutsche Apotheker Zeitung (**2001**), 141(25), 76-78
CODEN: DAZEA2; ISSN: 0011-9857
PUBLISHER: Deutscher Apotheker Verlag
DOCUMENT TYPE: Journal; General Review
LANGUAGE: German
AB A review with 5 refs. is given on mol. targeting as a strategy for the struggle against malaria, fatty acid biosynthesis in Plasmodium, and the effect of triclosan as a specific inhibitor of the enoyl-acyl carrier protein (ACP)-reductase.
ED Entered STN: 19 Jul 2001
IT **3380-34-5**, Triclosan
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(triclosan against malaria)
RN 3380-34-5 HCAPLUS
CN Phenol, 5-chloro-2-(2,4-dichlorophenoxy)- (7CI, 8CI, 9CI) (CA INDEX NAME)



CC 1-0 (Pharmacology)
IT **Antimalarials**
Drug targeting
(triclosan against malaria)
IT **3380-34-5**, Triclosan
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(triclosan against malaria)
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L181 ANSWER 9 OF 71 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 16
ACCESSION NUMBER: 1988:147032 HCAPLUS
DOCUMENT NUMBER: 108:147032
TITLE: Correlation of the efficiency of **fatty acid** derivatives in suppressing Plasmodium falciparum growth in culture with their **inhibitory** effect on acyl-CoA **synthetase** activity
AUTHOR(S): Beaumelle, Bruno D.; Vial, Henri J.
CORPORATE SOURCE: INSERM, Montpellier, 34090, Fr.
SOURCE: Molecular and Biochemical Parasitology (**1988**), 28(1), 39-42
CODEN: MBIPDP; ISSN: 0166-6851
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The intraerythrocytic malaria parasite depends on the surrounding medium for a supply of phospholipid precursors. Efficient inhibition (IC50 7-90 μM) of P. falciparum growth in vitro was achieved using modified fatty acids. The fatty acid analogs most effective in suppressing P. falciparum growth in culture were also the most active inhibitors of acyl-CoA synthetase from the monkey parasite P. knowlesi.
ED Entered STN: 30 Apr 1988
IT **141-22-0 20290-75-9**
RL: BIOL (Biological study)
(Plasmodium falciparum **inhibition** by, acyl-CoA **synthetase** in relation to)
RN 141-22-0 HCAPLUS
CN 9-Octadecenoic acid, 12-hydroxy-, (9Z,12R)- (9CI) (CA INDEX NAME)

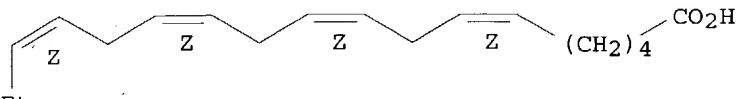
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 20290-75-9 HCAPLUS

CN 6,9,12,15-Octadecatetraenoic acid, (6Z,9Z,12Z,15Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



CC 10-5 (Microbial Biochemistry)
ST Plasmodium **fatty acid** acyl coenzyme synthetase; antimalarial action **fatty acid** deriv
IT **Antimalarials**
(**fatty acid** derivs.)
IT **Plasmodium falciparum**
(**inhibition** of, by **fatty acid** derivs., acyl-CoA **synthetase** in relation to)
IT **Fatty acids, biological studies**
RL: BIOL (Biological study)
(Plasmodium falciparum **inhibition** by derivs. of, acyl-CoA **synthetase** in relation to)
IT **Microbicidal and microbiostatic action**
(**antimalarial**, of **fatty acid** derivs.)
IT 9013-18-7, Acyl-CoA **synthetase**
RL: PROC (Process)
(**fatty acid** derivs. **inhibition** of, antimalarial activity in relation to)
IT **141-22-0** 764-67-0 18263-25-7 **20290-75-9** 29545-48-0, 5-Doxylstearate 53034-38-1
RL: BIOL (Biological study)
(Plasmodium falciparum **inhibition** by, acyl-CoA **synthetase** in relation to)

L181 ANSWER 10 OF 71 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:356269 HCAPLUS
DOCUMENT NUMBER: 138:348761
TITLE: Type 4 phosphodiesterase inhibitors and therapeutic uses thereof
INVENTOR(S): Eggenweiler, Hans-Michael; Wolf, Michael
PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany
SOURCE: PCT Int. Appl., 122 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003037349	A1	20030508	WO 2002-EP9596	20020828 <--

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF,

CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
EP 1463509 A1 20041006 EP 2002-802281 20020828 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK
PRIORITY APPLN. INFO.: EP 2001-125394 A 20011031 <--
WO 2002-EP9596 W 20020828

OTHER SOURCE(S): MARPAT 138:348761

AB The invention discloses the use of type 4 phosphodiesterase inhibitors (PDE IV inhibitors) to treat diseases, as well as combinations of PDE IV inhibitors with other drugs.

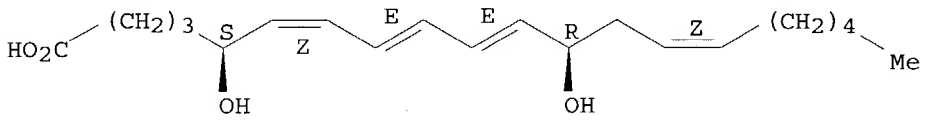
ED Entered STN: 09 May 2003

IT **71160-24-2**, LTB4 **72025-60-6**, LTC4 **73836-78-9**, LTD4 **75715-89-8**, LTE4
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonists; phosphodiesterase IV inhibitors, therapeutic uses, and use with other agents)

RN 71160-24-2 HCAPLUS

CN 6,8,10,14-Eicosatetraenoic acid, 5,12-dihydroxy-, (5S,6Z,8E,10E,12R,14Z)-(9CI) (CA INDEX NAME)

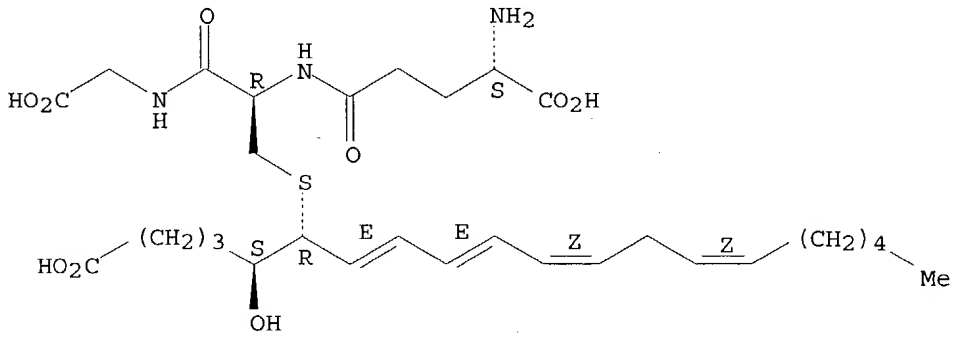
Absolute stereochemistry.
Double bond geometry as shown.



RN 72025-60-6 HCAPLUS

CN Glycine, L-γ-glutamyl-S-[(1R,2E,4E,6Z,9Z)-1-[(1S)-4-carboxy-1-hydroxybutyl]-2,4,6,9-pentadecatetraenyl]-L-cysteinyl- (9CI) (CA INDEX NAME)

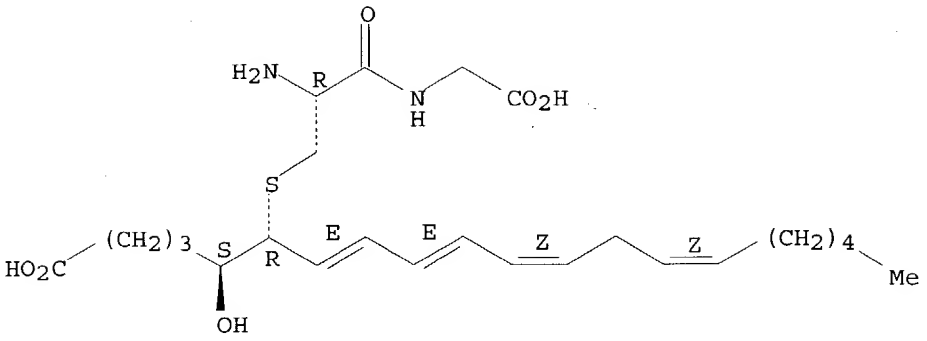
Absolute stereochemistry.
Double bond geometry as shown.



RN 73836-78-9 HCAPLUS

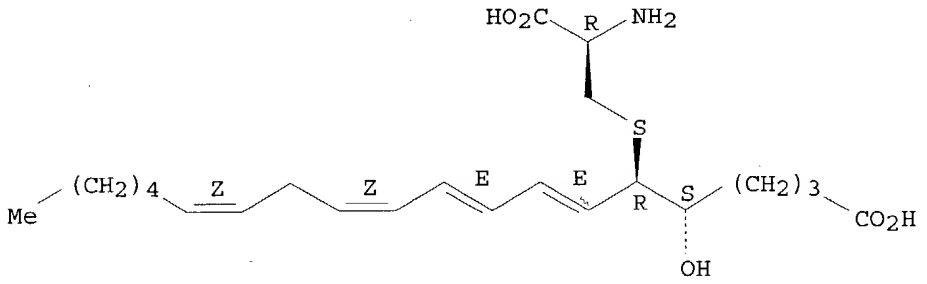
CN Glycine, S-[(1R,2E,4E,6Z,9Z)-1-[(1S)-4-carboxy-1-hydroxybutyl]-2,4,6,9-pentadecatetraenyl]-L-cysteinyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 75715-89-8 HCAPLUS
CN 7,9,11,14-Eicosatetraenoic acid, 6-[[(2R)-2-amino-2-carboxyethyl]thio]-5-hydroxy-, (5S,6R,7E,9E,11Z,14Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



IC ICM A61K031-54
ICS A61K031-495; A61K031-50; A61P011-06; A61P017-06; A61P029-00; A61P037-00
CC 1-12 (Pharmacology)
IT **Leukotrienes**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**biosynthesis, inhibitors**; phosphodiesterase IV **inhibitors**, therapeutic uses, and use with other agents)
IT **Malaria**
(malarial cachexia; phosphodiesterase IV inhibitors, therapeutic uses, and use with other agents)
IT 65154-06-5, Platelet-activating factor **71160-24-2**, LTB4 **72025-60-6**, LTC4 **73836-78-9**, LTD4 **75715-89-8**, LTE4
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonists; phosphodiesterase IV inhibitors, therapeutic uses, and use with other agents)
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L181 ANSWER 11 OF 71 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:817930 HCAPLUS
DOCUMENT NUMBER: 139:318706
TITLE: Antimicrobial compositions containing chemically-modified peptides
INVENTOR(S): Kuhner, Carla H.; Romesser, James A.

PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 34 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003194445	A1	20031016	US 2001-5931	20011112 <--
WO 2003091276	A2	20031106	WO 2002-US35066	20021031 <--
WO 2003091276	A3	20041007		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1480664	A2	20041201	EP 2002-807320	20021031 <--

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK

PRIORITY APPLN. INFO.:	US 2001-5931	A	20011112 <--
	WO 2002-US35066	W	20021031

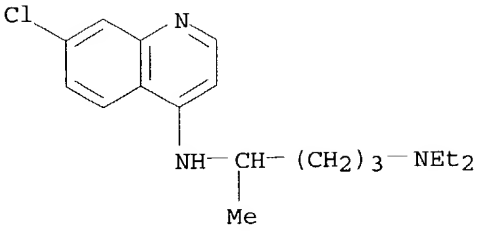
AB Peptide compns. and methods for inhibiting and controlling the growth of microbes using peptides possessing antimicrobial activity are described. The composition comprises at least one antimicrobial peptide in combination with at least one biocide, germicide, preservative or antibiotic. The method comprises administering an amount of the peptide composition effective for the prevention, inhibition or termination of microbes in industrial and clin. settings. An antimicrobial composition comprises at least one chemical-modified peptide and a second antimicrobial compound, wherein said chemical-modified peptide is represented by formula R1C(:O)XnNH21 (X = (non-)natural (un)modified amino acid, except glutamate or aspartate; n = 1 to 5; (a) when said chemical-modified peptide is 1-3 amino acids, at least one amino acid is a cationic amino acid, the net charge of said peptide at neutral pH is at least +1, and said chemical-modified peptide does not contain glutamate or aspartate; (b) when said chemical-modified peptide is 4-5 amino acids, at least two of the amino acids are cationic amino acids, the net charge of said peptide at neutral pH is at least +2, and said chemical-modified peptide does not contain glutamate or aspartate; R1 = C1-C20 alkyl, C3-C6 cycloalkyl, C4-C20 alkenyl, C4-C20 alkynyl, etc.).

ED Entered STN: 17 Oct 2003

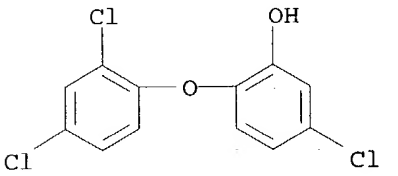
IT **54-05-7**, Chloroquine **3380-34-5**, 2,4,4' Trichloro-2'-hydroxydiphenylether
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(addnl. antimicrobial compound in antimicrobial compns. containing chemical-modified peptides)

RN 54-05-7 HCAPLUS

CN 1,4-Pentanediamine, N4-(7-chloro-4-quinolinyl)-N1,N1-diethyl- (9CI) (CA INDEX NAME)



RN 3380-34-5 HCAPLUS
CN Phenol, 5-chloro-2-(2,4-dichlorophenoxy)- (7CI, 8CI, 9CI) (CA INDEX NAME)



IC ICM A01N055-02
ICS A01N043-80; A01N043-50; A01N047-40; A01N047-46
NCL 424622000; 514017000; 514018000; 514019000; 424661000; 514372000; 514389000; 514184000; 514514000; 514634000
CC 5-2 (Agrochemical Bioregulators)
Section cross-reference(s): 63
IT 51-17-2, Benzimidazole 52-51-7, 2-Bromo-2-nitropropane-1,3-diol **54-05-7**, Chloroquine 56-75-7, Chloramphenicol 60-54-8, Tetracycline 74-55-5, Ethambutol 88-04-0, Chloroxylenol 90-34-6, Primaquine 94-36-0, Benzoyl peroxide, biological studies 100-33-4, Pentamidine 100-97-0, Methenamine, biological studies 101-20-2, 1-(4-Chlorophenyl)-3-(3,4-dichlorophenyl) urea 111-30-8, Glutaraldehyde 151-21-3, Sodium lauryl sulfate, biological studies 288-32-4D, Imidazole, derivs. 443-48-1, Metronidazole 461-72-3D, Hydantoin, halo derivs. 463-77-4, Carbamic acid, biological studies 504-76-7D, Oxazolidine, derivs. 659-40-5, Hexamidine diisethionate 738-70-5, Trimethoprim 1406-05-9, Penicillin 1875-92-9D, Dimethylbenzylammonium chloride, n-alkyl derivative 2682-20-4, 2-Methyl-4-isothiazolin-3-one **3380-34-5**, 2,4,4' Trichloro-2'-hydroxydiphenylether 3697-42-5, Chlorhexidine hydrochloride 6317-18-6, Methylene bis(thiocyanate) 7166-19-0, .β.-Bromo-.β.-nitrostyrene 7647-15-6, Sodium bromide, biological studies 7681-52-9, Sodium hypochlorite 7778-41-8D, chromated 7778-54-3, Calcium hypochlorite 10222-01-2, 2,2-Dibromo-3-nitrilo propionamide 11006-76-1, Streptogramin 11111-12-9, Cephalosporin 13292-46-1, Rifampin 13463-41-7, Zinc pyrithione 13590-97-1, Dodecylguanidine hydrochloride 23155-02-4, Fosfomycin 26172-55-4, 5-Chloro-2-methyl-4-isothiazolin-3-one 29656-58-4, Hydroxybenzoic acid 36791-04-5, Ribavirin 37205-61-1, Protease inhibitor 37306-44-8D, Triazole, derivs. 37338-39-9 39660-61-2, Isopropylmethylphenol 55268-74-1, Praziquantel 59277-89-3, Acyclovir 68890-66-4, Octopirox 80738-43-8, Lincosamide 82280-72-6, Dinonylsulfosuccinate 83200-96-8, Carbapenem 154592-20-8, Copper pyrithione
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(addnl. antimicrobial compound in antimicrobial compns. containing chemical-modified peptides)

L181 ANSWER 12 OF 71 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:487338 HCAPLUS
DOCUMENT NUMBER: 137:59514
TITLE: Cloning and sequencing of Plasmodium falciparum Fab I (enoyl acyl carrier protein reductase) gene and method for inhibition of apicomplexan parasites
INVENTOR(S): McLeod, Rima; Muench, Stephen P.; Rafferty, John B.; Kyle, Dennis E.; Mui, Ernest J.; Kirisits, Michael J.; Mack, Douglas G.; Roberts, Craig W.; Samuel, Benjamin U.; Lyons, Russel E.; Milhous, Wilbur K.; Rice, David W.; Prigge, Sean
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2002049576	A2	20020627	WO 2001-US49738		20011220 <--
WO 2002049576	C2	20030424			
WO 2002049576	A3	20020912			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2432992	AA	20020627	CA 2001-2432992		20011220 <--
AU 2002037731	A5	20020701	AU 2002-37731		20011220 <--
EP 1363654	A2	20031126	EP 2001-986546		20011220 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
US 2004137446	A1	20040715	US 2003-465527		20030618 <--
PRIORITY APPLN. INFO.:			US 2000-257771P	P	20001221 <--
			US 2001-264499P	P	20010126 <--
			WO 2001-US49738	W	20011220 <--

AB The present invention relates the first report of apicomplexan Fab I, enoyl acyl carrier protein reductase (ENR), and discloses the effects of triclosan, a potent and specific inhibitor of this enzyme, on the in vitro growth of Toxoplasma gondii and Plasmodium falciparum. A plant-like Fab I in P. falciparum was identified by the inventors and the structure was modeled on the Brassia napus and Escherichia coli structures, alone and complexed to triclosan (5-chloro-2-[2,4 dichloropheoxyl] phenol), which confirmed all the requisite features of an ENR. Triclosan markedly inhibits growth and survival of the apicomplexan parasites P. falciparum and T. gondii at low concns. Initially, a sequence for a P. falciparum Fab I was located on the aggregate P. falciparum chromosomes referred to as "blob". The P. falciparum Fab I nucleotide and deduced amino acid sequence (GenBank Accession Number AF338731) and a multisequence alignment with representative ENRs are provided. Discovery and characterization of an apicomplexan Fab I gene and encoded enzyme and discovery of the triclosan as a lead compound, provide means to rationally design novel

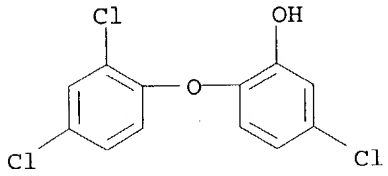
inhibitory compns. useful for prevention and treatment of apicomplexan related diseases.

ED Entered STN: 28 Jun 2002

IT **3380-34-5**, Triclosan
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as specific inhibitor of Fab I, use to inhibit apicomplexan growth and survival; cloning and sequencing of Plasmodium falciparum Fab I (enoyl acyl carrier protein reductase) gene and method for inhibition of apicomplexan parasites)

RN 3380-34-5 HCAPLUS

CN Phenol, 5-chloro-2-(2,4-dichlorophenoxy)- (7CI, 8CI, 9CI) (CA INDEX NAME)



IC ICM A61K

CC 7-3 (Enzymes)
Section cross-reference(s): 1, 3, 10

IT **Plasmodium falciparum**
Toxoplasma gondii
(triclosan as specific inhibitor of Fab I from; cloning and sequencing of Plasmodium falciparum Fab I (enoyl acyl carrier protein reductase) gene and method for inhibition of apicomplexan parasites)

IT **3380-34-5**, Triclosan
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as specific inhibitor of Fab I, use to inhibit apicomplexan growth and survival; cloning and sequencing of Plasmodium falciparum Fab I (enoyl acyl carrier protein reductase) gene and method for inhibition of apicomplexan parasites)

L181 ANSWER 13 OF 71 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:671827 HCAPLUS
DOCUMENT NUMBER: 137:206549
TITLE: Absorbable solid compositions for topical treatment of oral mucosal disorders
INVENTOR(S): Domb, Avraham J.; Wolnerman, Joseph Simcha
PATENT ASSIGNEE(S): Efrat Biopolymers Ltd., Israel
SOURCE: Eur. Pat. Appl., 25 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1236466	A1	20020904	EP 2002-251320	20020226 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2003003140	A1	20030102	US 2002-83413	20020227 <--

PRIORITY APPLN. INFO.: US 2001-271735P P 20010228 <--

AB A solid, self-bioadhesive composition is provided for topical application that

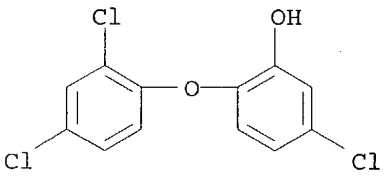
adheres to the oral mucosal tissue comprising a therapeutically effective amount of at least one herbal or homeopathic active agent and a pharmaceutically acceptable solid bioadhesive carrier in an amount of about 40-99% based on the weight of the whole composition A herbal agent is selected from bioactive herb exts., tinctures and essential oils. The composition further comprises a non-herbal active agent, e.g., analgesics, anti-inflammatory agents, antihistaminics, antiallergics, antimicrobial drugs, vitamins, enzymes, etc. For example, tablets were prepared by compression molding of herbal and non-herbal actives in powder form and mixts. of Carbopol 934 and HPMC. The formulation contained a herbal powder (an equal ratio of Echinacea, Calendula and golden seal exts.) 10 mg, vancomycin 1 mg, Carbopol 934 50 mg, and mint extract 5 mg. The cap coating was composed of a mixture of 5 mg of Mg-stearate and 5 mg Carbopol/HPMC (2:1 by weight). The preparation was used by patients exhibiting herpetic stomatitis lesions, aphthous ulcers, mucosal inflammation, toothache, RAS, and lesions on the lips, tang, and gingiva.

ED Entered STN: 06 Sep 2002

IT **3380-34-5**, Triclosan
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(absorbable solid compns. for topical treatment of oral mucosal disorders)

RN 3380-34-5 HCAPLUS

CN Phenol, 5-chloro-2-(2,4-dichlorophenoxy)- (7CI, 8CI, 9CI) (CA INDEX NAME)



IC ICM A61K009-00

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1

IT Allergy inhibitors
Analgesics
Angelica
Anti-inflammatory agents
Antibacterial agents
Antibiotics
Antihistamines
Antimalarials
Antimicrobial agents
Antipyretics
Antiulcer agents
Antiviral agents
Baptisia
Calendula
Centella asiatica
Coneflower
Crataegus
Cytotoxic agents
Disinfectants
Echinacea
Fungicides
Glycyrrhiza
Human
Human herpesvirus

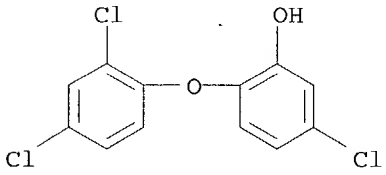
Hydrastis canadensis
Hypericum
Krameria
Malva
Matricaria
Parasiticides
Phytolacca
Plantago
Plasmid vectors
Propolis
Rosmarinus officinalis
Salvia
Salvia officinalis
Sambucus
Styrax
Taraxacum
Tsuga
Uncaria
(absorbable solid compns. for topical treatment of oral mucosal disorders)

IT 50-02-2, Dexamethasone 50-23-7, Hydrocortisone 50-36-2, Cocaine 55-56-1, Chlorhexidine 59-46-1, Procaine 60-54-8, Tetracycline 68-35-9, Sulfadiazine 73-40-5, Guanine 75-47-8, Iodoform 76-22-2, Camphor 76-57-3, Codeine 79-10-7D, Acrylic acid, esters, polymers 79-41-4D, Methacrylic acid, esters, polymers 85-79-0, Dibucaine 94-09-7, Benzocaine 94-24-6, Tetracaine 96-88-8, Mepivacaine 99-96-7D, p-Hydroxybenzoic acid, esters 108-95-2, Phenol, biological studies 124-94-7, Triamcinolone 133-16-4, Chloroprocaine 137-58-6, Lidocaine 138-86-3, Limonene 288-88-0, 1H-1,2,4-Triazole 586-60-7, Dyclonine 721-50-6, Prilocaine 738-70-5, Trimethoprim 1318-27-0, Carnallite 1397-89-3, Amphotericin B 1400-61-9, Nystatin **3380-34-5**, Triclosan 6277-14-1, Acetoxolone 6809-52-5, Teprenone 7447-40-7, Potassium chloride, biological studies 7631-86-9, Silica, biological studies 7647-14-5, Sodium chloride, biological studies 7681-49-4, Sodium fluoride, biological studies 7789-48-2, Magnesium bromide 9000-30-0, Guar-gum 9000-69-5, Pectin 9002-89-5, Poly(vinyl alcohol) 9003-01-4, Poly(acrylic acid) 9004-32-4, Carboxymethyl cellulose sodium 9004-34-6D, Cellulose, derivs. 9004-54-0, Dextran, biological studies 9004-61-9, Hyaluronic acid 9004-62-0, Hydroxyethyl cellulose 9004-64-2, Hydroxypropyl cellulose 9004-65-3, Hydroxypropyl methyl cellulose 9005-25-8D, Starch, derivs. 9007-16-3, Carbopol 934 9025-70-1, Dextranase 9036-66-2, Arabinogalactan 9057-02-7, Pullulan 13463-67-7, Titanium dioxide, biological studies 14807-96-6, Talc, biological studies 15687-27-1, Ibuprofen 22916-47-8, Miconazole 25322-68-3, Polyethylene oxide 25655-41-8, Povidone-iodine 27254-80-4, Acridinamine 36637-18-0, Etidocaine 38396-39-3, Bupivacaine 54182-58-0, Sucralfate 59277-89-3, Acyclovir 73590-58-6, Omeprazole 76050-42-5, Carbopol 940 82419-36-1, Ofloxacin 84625-61-6, Itraconazole
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(absorbable solid compns. for topical treatment of oral mucosal disorders)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L181 ANSWER 14 OF 71 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:342801 HCAPLUS
DOCUMENT NUMBER: 138:66181
TITLE: Triclosan offers protection against blood stages of malaria by inhibiting enoyl-ACP reductase of

Plasmodium falciparum. [Erratum to document cited in CA134:290011]
AUTHOR(S): Surolia, Namita; Surolia, Avadhesha
CORPORATE SOURCE: Molecular Biology and genetics Unit, Jawaharlat Nehru Centre for Advanced Scientific Research, Jakkur, Bangalore, India
SOURCE: Nature Medicine (New York, NY, United States) (**2001**), 7(5), 636
CODEN: NAMEFI; ISSN: 1078-8956
PUBLISHER: Nature America Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB On page 167, the sentence beginning "Cerulenin, an antibiotic and a non-competitive inhibitor of fatty acid synthase11" should cite reference 10 instead of 11. On page 168, the following sentence was omitted from the end of the second paragraph: "Mouse lymphocytes exhibited normal morphol. and growth patterns in the presence of the drug.". In Figure 3d, the fourth bar of the histogram should indicate 8 μm triclosan instead of 18 μm.
ED Entered STN: 14 May 2001
IT **3380-34-5**, Triclosan
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(triclosan protects against blood stages of malaria by inhibiting enol-ACP reductase of Plasmodium falciparum (Erratum))
RN 3380-34-5 HCAPLUS
CN Phenol, 5-chloro-2-(2,4-dichlorophenoxy)- (7CI, 8CI, 9CI) (CA INDEX NAME)



CC 1-5 (Pharmacology)
Section cross-reference(s): 10
IT **Fatty acids, biological studies**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**synthesis**; triclosan protects against blood stages of malaria by **inhibiting** enol-ACP reductase of Plasmodium falciparum (Erratum))
IT **Antimalarials**
Plasmodium (malarial genus)
(triclosan protects against blood stages of malaria by inhibiting enol-ACP reductase of Plasmodium falciparum (Erratum))
IT **3380-34-5**, Triclosan
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(triclosan protects against blood stages of malaria by inhibiting enol-ACP reductase of Plasmodium falciparum (Erratum))

L181 ANSWER 15 OF 71 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:268334 HCAPLUS
DOCUMENT NUMBER: 129:8587
TITLE: Method and compositions for disrupting the epithelial

barrier function

INVENTOR(S): Elias, Peter M.; Feingold, Kenneth R.; Holleran, Walter M.; Thornfeldt, Carl R.

PATENT ASSIGNEE(S): Regents of the University of California, USA; Cellegy Pharmaceuticals, Inc.

SOURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9817253	A1	19980430	WO 1997-US19343	19971022 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9749193	A1	19980515	AU 1997-49193	19971022 <--
US 6190894	B1	20010220	US 1998-58401	19980409 <--
US 6562606	B1	20030513	US 2000-608568	20000630 <--

PRIORITY APPLN. INFO.:

US 1996-733712	A	19961023 <--
US 1993-33811	B2	19930319 <--
US 1994-260559	B2	19940616 <--
WO 1997-US19343	W	19971022 <--
US 1998-58401	A1	19980409 <--

AB Epithelial barrier function is disrupted in a host in need of topical administration of a physiol. active substance by applying to the epithelium a barrier-disrupting amount of ≥1 agent selected from (1) inhibitors of synthesis of ceramides, acylceramides, glucosylceramides, sphingomyelins, fatty acids, or cholesterol; (2) degradation enzymes for ceramides, acylceramides, glucosylceramides, or sphingomyelins; (3) inhibitors of degradation of phospholipids, glycosphingolipids, glucosylceramides, acylceramides, or sphingomyelins; and (4) inhibitors and stimulators of metabolic enzymes of free fatty acids, ceramides, and cholesterol. Thus, a combination of 5-tetradecyloxy-2-furancarboxylic acid (an inhibitor of acetyl-CoA carboxylase which is the rate-limiting enzyme in free fatty acid synthesis) and β-chloroalanine (an inhibitor of serine palmitoyltransferase, the rate-limiting enzyme in ceramide synthesis) increased delivery of lidocaine through mouse stratum corneum by 8-fold in vivo and increased transepidermal water loss. Thus, a combination of 5-tetradecyloxy-2-furancarboxylic acid (an inhibitor of acetyl-CoA carboxylase which is the rate-limiting enzyme in free fatty acid synthesis) and β-chloroalanine (an inhibitor of serine palmitoyltransferase, the rate-limiting enzyme in ceramide synthesis) increased delivery of lidocaine through mouse stratum corneum by 8-fold in vivo and increased transepidermal water loss.

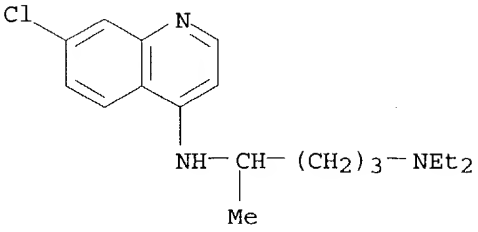
ED Entered STN: 11 May 1998

IT **54-05-7**, Chloroquine **303-43-5**, Cholesterol oleate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method and compns. for disrupting the epithelial barrier function)

RN 54-05-7 HCAPLUS

CN 1,4-Pentanediamine, N4-(7-chloro-4-quinolinyl)-N1,N1-diethyl- (9CI) (CA

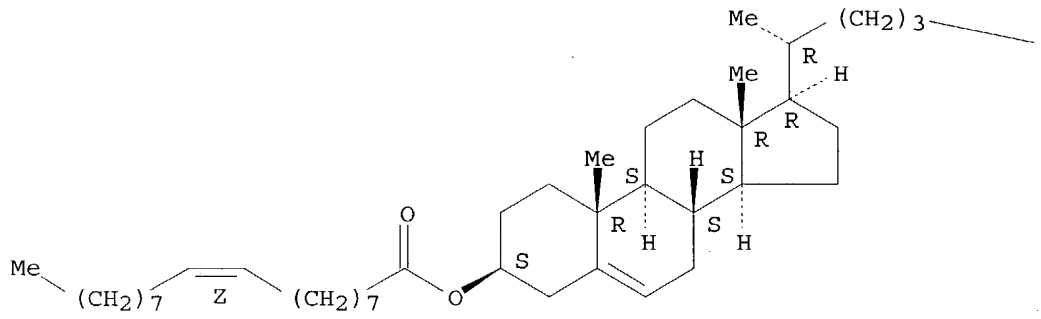
INDEX NAME)



RN 303-43-5 HCAPLUS
CN Cholest-5-en-3-ol (3β)-, (9Z)-9-octadecenoate (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

CHMe2

IC ICM A61K009-10
CC 63-6 (Pharmaceuticals)
IT Ceramides
Fatty acids, biological studies
Glycosphingolipids
Phospholipids, biological studies
Sphingomyelins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(metabolism of, inhibitors of; method and compns. for disrupting the epithelial barrier function)
IT **Antimalarials**
Epithelium
Permeation enhancers
(method and compns. for disrupting the epithelial barrier function)
IT 9001-22-3, β-Glucosidase 9001-62-1 9001-84-7, Phospholipase A 9013-93-8, Phospholipase 9023-93-2, Acetyl-CoA carboxylase 9028-35-7 9029-62-3, Squalene epoxidase 9031-48-5, Glucosyltransferase 9031-54-3, Sphingomyelinase 9033-57-2 9045-77-6, **Fatty**

acid synthetase 9077-14-9, Squalene synthetase
9080-21-1 37257-09-3, Ceramide synthetase 55467-49-7 58703-97-2,
Phosphatidylcholine-ceramide phosphorylcholine transferase 62213-50-7,
Serine palmitoyltransferase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**inhibitors**; method and compns. for **disrupting** the
epithelial barrier function)

IT 50-02-2, Dexamethasone 50-24-8, Prednisolone 50-47-5, Desipramine
50-49-7, Imipramine 50-53-3, Chlorpromazine, biological studies
52-53-9, Verapamil 53-86-1, Indomethacin **54-05-7**, Chloroquine
54-64-8, Thimerosal 57-55-6, Propylene glycol, biological studies
57-88-5D, Cholesterol, esters 67-42-5, EGTA 67-68-5, DMSO, biological
studies 68-41-7, D-Cycloserine 78-41-1, Triparanol 83-89-6,
Quinacrine 84-97-9D, Perazine, chloro derivs. 85-79-0, Dibucaine
92-84-2D, Phenothiazine, derivs. 98-80-6, Phenylboronic acid 99-73-0
111-58-0, N-Oleoylethanolamine 117-39-5, Quercetin 117-89-5,
Trifluoperazine 118-42-3, Hydroxychloroquine 123-78-4D, Sphingosine,
hexylglucosyl derivs. 137-58-6, Lidocaine 143-28-2, Oleyl alcohol
270-26-8, 7H-1,3-Dioxolo[4,5-h][3]benzazepine 302-79-4,
all-trans-Retinoic acid **303-43-5**, Cholesterol oleate 313-05-3,
20,25-Diazacholesterol 339-72-0, L-Cycloserine 362-74-3, Dibutyryl
cyclic AMP 366-93-8, AY 9944 390-64-7 481-49-2, Cepharanthine
525-66-6, Propranolol 526-87-4, Conduritol 872-50-4,
N-Methylpyrrolidin-2-one, biological studies 1154-25-2 1256-86-6,
Cholesterol sulfate 1393-88-0, Gramicidin D 1403-66-3, Gentamicin
1404-04-2, Neomycin 2001-96-9 2140-46-7, 25-Hydroxycholesterol
3821-81-6, β-Fluoroalanine 3981-36-0, β-Chloroalanine
4358-16-1, Cholesterol phosphate 4759-48-2, 13-cis-Retinoic acid
6090-95-5, Conduritol B-epoxide 6734-33-4 7287-36-7, Monalide
9034-40-6, LHRH 10238-27-4 10238-28-5 13095-61-9,
26-Hydroxycholesterol 13780-71-7, Boronic acid 19130-96-2,
Deoxynojirimycin 21829-25-4, Nifedipine 22204-53-1, Naproxen
24579-86-0 24887-57-8, 22,25-Diazacholesterol 25265-75-2, Butanediol
25496-72-4, Glycerol monooleate 27848-84-6, Nicergoline 36894-69-6,
Labetalol 42399-41-7, Diltiazem 54857-86-2, 5-Tetradecyloxy-2-
furancarboxylic acid 55985-32-5, Nicardipine 57265-65-3, R-24571
58546-54-6, Gomisin A 59227-89-3, 1-Dodecylazacycloheptan-2-one
59865-13-3, Cyclosporin A 65595-90-6 66085-59-4, Nimodipine
67655-93-0, Esterastin 73573-88-3, Mevastatin 75330-75-5, Lovastatin
79902-63-9, Simvastatin 81093-37-0, Pravastatin 93957-55-2,
Fluindostatin 96829-58-2, Tetrahydrolipstatin 116355-83-0, Fumonisin
B1 117019-08-6 126661-83-4, Cyclophellitol 159440-05-8 159440-26-3
194038-29-4 207351-39-1 207351-40-4 207351-41-5 207351-42-6
207351-43-7
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)
(method and compns. for disrupting the epithelial barrier function)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L181 ANSWER 16 OF 71 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:455070 HCAPLUS
DOCUMENT NUMBER: 122:204844
TITLE: Chloroquine inhibits stimulated platelets at the arachidonic acid pathway
AUTHOR(S): Nosal, Rado; Jancinova, Viera; Petrikova, Margita
CORPORATE SOURCE: Inst. Experimental Pharmacology, Slovak Academy Sciences, Bratislava, Slovakia
SOURCE: Thrombosis Research (**1995**), 77(6), 531-42

CODEN: THBRAA; ISSN: 0049-3848
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

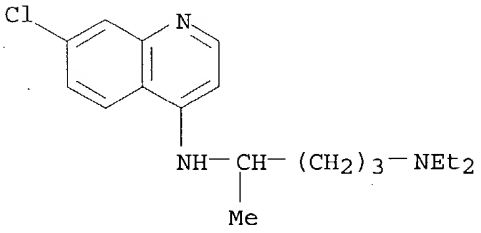
AB Chloroquine inhibited arachidonic acid liberation from membrane phospholipids of thrombin- and A23187-stimulated platelets. In addition, it dose-dependently inhibited stimulated malondialdehyde formation and thromboxane B2 generation in the same platelets. The linear correlation between the inhibition of arachidonic acid liberation and malondialdehyde formation indicated that chloroquine inhibited activated phospholipase A2 in thrombin-stimulated platelets, similarly as it does in different cells and tissues. Yet, the nonlinear relationship between arachidonic acid liberation along with malondialdehyde formation and thromboxane generation as well as aggregation suggest that phospholipase A2 does not seem to be the only site of chloroquine action. Rather, it may affect platelets either at other levels of the arachidonic acid cascade too, or at some different stimulatory pathways, like intraplatelet calcium mobilisation, phosphoinositide cycle, calmodulin and protein kinase C activation.

ED Entered STN: 31 Mar 1995

IT **54-05-7**, Chloroquine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chloroquine inhibits stimulated platelets at arachidonic acid pathway)

RN 54-05-7 HCAPLUS

CN 1,4-Pentanediamine, N4-(7-chloro-4-quinolinyl)-N1,N1-diethyl- (9CI) (CA INDEX NAME)

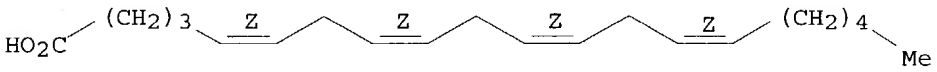


IT **506-32-1**, Arachidonic acid
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(chloroquine inhibits stimulated platelets at arachidonic acid pathway)

RN 506-32-1 HCAPLUS

CN 5,8,11,14-Eicosatetraenoic acid, (5Z,8Z,11Z,14Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



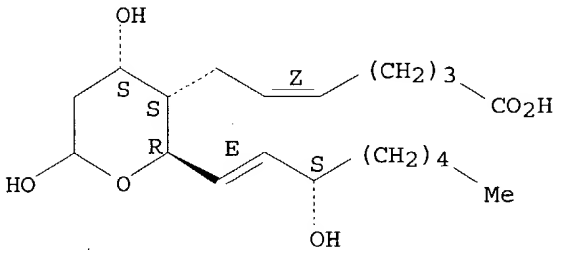
IT **54397-85-2**, Thromboxane B2
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**generation**; chloroquine **inhibits** stimulated platelets at arachidonic acid pathway)

RN 54397-85-2 HCAPLUS

CN 5-Heptenoic acid, 7-[(2R,3S,4S)-tetrahydro-4,6-dihydroxy-2-[(1E,3S)-3-

hydroxy-1-octenyl]-2H-pyran-3-yl]-, (5Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



CC 1-8 (Pharmacology)
IT **54-05-7**, Chloroquine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chloroquine inhibits stimulated platelets at arachidonic acid pathway)
IT **506-32-1**, Arachidonic acid
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(chloroquine inhibits stimulated platelets at arachidonic acid pathway)
IT **54397-85-2**, Thromboxane B2
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**generation**; chloroquine **inhibits** stimulated platelets at arachidonic acid pathway)

L181 ANSWER 17 OF 71 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1993:503333 HCAPLUS
DOCUMENT NUMBER: 119:103333
TITLE: Enhanced skin penetration system for improved topical delivery of drugs
INVENTOR(S): Deckner, George Endel; Lombardo, Brian Scott
PATENT ASSIGNEE(S): Richardson-Vicks, Inc., USA
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9307903	A1	19930429	WO 1992-US8744	19921013 <--
W: AU, BB, BG, BR, CA, CS, FI, HU, JP, KP, KR, LK, MG, MN, MW, NO, PL, RO, RU, SD				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG				
AU 9228639	A1	19930521	AU 1992-28639	19921013 <--
AU 675212	B2	19970130		
EP 608322	A1	19940803	EP 1992-921769	19921013 <--
EP 608322	B1	19980722		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, SE				
JP 07500594	T2	19950119	JP 1993-507771	19921013 <--
JP 3471354	B2	20031202		

HU 67046	A2	19950130	HU 1994-1106	19921013 <--
BR 9206631	A	19951024	BR 1992-6631	19921013 <--
AT 168563	E	19980815	AT 1992-921769	19921013 <--
ES 2118834	T3	19981001	ES 1992-921769	19921013 <--
CA 2117265	C	20000801	CA 1992-2117265	19921013 <--
CN 1072602	A	19930602	CN 1992-113328	19921016 <--
CN 1050763	B	20000329		
US 6277892	B1	20010821	US 1994-191734	19940204 <--
NO 9401317	A	19940616	NO 1994-1317	19940413 <--
FI 9401770	A	19940415	FI 1994-1770	19940415 <--
HK 1013002	A1	20000623	HK 1998-114300	19981221 <--
PRIORITY APPLN. INFO.:			US 1991-778422 A	19911016 <--
			US 1992-948391 A	19920925 <--
			WO 1992-US8744 A	19921013 <--
			US 1993-59001 B1	19930506 <--

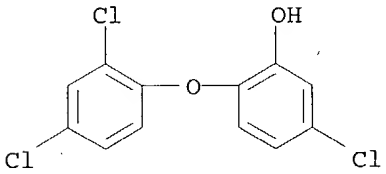
AB A topical composition with enhanced penetration through skin comprises an active agent and a high-mol.-weight crosslinked cationic polymer, such as dialkylaminoalkyl (meth)acrylate polymers. An anti-acne composition contained Alc. SDA-40 40.0, Polyquaternium-32 and mineral oil 4.0, salicylic acid 2.0, and purified water 54.0%.

ED Entered STN: 04 Sep 1993

IT **3380-34-5**, Triclosan
RL: BIOL (Biological study)
(antimicrobial topical compns. containing dialkylaminoalkyl acrylate polymers and)

RN 3380-34-5 HCAPLUS

CN Phenol, 5-chloro-2-(2,4-dichlorophenoxy)- (7CI, 8CI, 9CI) (CA INDEX NAME)



IC ICM A61K047-32
ICS A61K007-48

CC 63-6 (Pharmaceuticals)

IT Anesthetics
Anti-infective agents
Antiarrhythmics
Antidepressants
Antiemetics
Antihistaminics
Antihypertensives
Antimalarials
Antitussives
Appetite depressants
Cardiotonics
Cholinergic agonists
Diuretics
Hypnotics and Sedatives
Inflammation inhibitors
Muscle relaxants
Neoplasm inhibitors
Nervous system stimulants
Sunscreens
Tranquilizers and Neuroleptics

Ulcer inhibitors
Vasoconstrictors
Vasodilators
Wound healing promoters
(topical compns. containing dialkylaminoalkyl acrylate polymers and)
IT 55-56-1, Chlorhexidine 57-62-5, Chlortetracycline 57-92-1, Streptomycin, biological studies 59-01-8, Kanamycin 74-55-5, Ethambutol 79-57-2, Oxytetracycline 100-33-4, Pentamidine 100-97-0, biological studies 154-21-2 443-48-1, Metronidazole 564-25-0 768-94-5, Tricyclo[3.3.1.13,7]decan-1-amine 914-00-1, Methacycline 1403-66-3, Gentamicin 1404-04-2, Neomycin **3380-34-5**, Triclosan 7542-37-2, Paromomycin 10118-90-8, Minocycline 11003-38-6, Capreomycin 22916-47-8, Miconazole 32986-56-4, Tobramycin 37517-28-5, Amikacin 56391-56-1, Netilmicin 70458-96-7, Norfloxacin 85721-33-1, Ciprofloxacin
RL: BIOL (Biological study)
(antimicrobial topical compns. containing dialkylaminoalkyl acrylate polymers and)

L181 ANSWER 18 OF 71 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1993:503334 HCAPLUS
DOCUMENT NUMBER: 119:103334
TITLE: Enhanced skin penetration system for improved topical delivery of drugs
INVENTOR(S): Deckner, George Endel; Lombardo, Brian Scott
PATENT ASSIGNEE(S): Richardson-Vicks, Inc., USA
SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9307902	A1	19930429	WO 1992-US8741	19921013 <--
W: AU, BB, BG, BR, CA, CS, FI, HU, JP, KP, KR, LK, MG, MN, MW, NO, PL, RO, RU, SD				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG				
AU 9228064	A1	19930521	AU 1992-28064	19921013 <--
AU 675211	B2	19970130		
EP 608320	A1	19940803	EP 1992-921755	19921013 <--
EP 608320	B1	19980128		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, SE				
HU 74560	A2	19970128	HU 1994-1107	19921013 <--
AT 162725	E	19980215	AT 1992-921755	19921013 <--
ES 2114569	T3	19980601	ES 1992-921755	19921013 <--
CN 1072863	A	19930609	CN 1992-112390	19921016 <--
IN 178157	A	19970308	IN 1992-DE1011	19921105 <--
IN 181010	A	19980411	IN 1992-DE1013	19921105 <--
NO 9401319	A	19940616	NO 1994-1319	19940413 <--
FI 9401771	A	19940415	FI 1994-1771	19940415 <--
US 5756118	A	19980526	US 1995-462258	19950605 <--
US 5756119	A	19980526	US 1995-462376	19950605 <--
US 5773023	A	19980630	US 1995-462710	19950605 <--
US 5780049	A	19980714	US 1995-464991	19950605 <--
US 5776485	A	19980707	US 1995-469701	19950606 <--
US 5874095	A	19990223	US 1998-49367	19980327 <--
PRIORITY APPLN. INFO.:			US 1991-778424 A	19911016 <--

US 1992-957752	B1	19921002 <--
WO 1992-US8741	A	19921013 <--
US 1993-111032	B1	19930824 <--
US 1994-228167	B1	19940415 <--
US 1995-390902	B3	19950216 <--
US 1995-462710	B3	19950605 <--

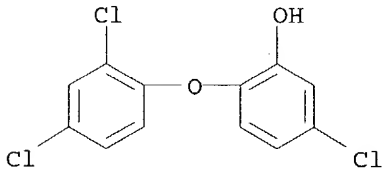
AB A topical composition with enhanced penetration through skin comprises an active agent and a nonionic polyacrylamide having a mol. weight of 1χ106-3χ107. An analgesic composition contained Alc. SDA-40 40.0, ibuprofen 2.0, polyacrylamide/C13-14 isoparaffin/Laureth-7 3.0, and purified water 55.0%.

ED Entered STN: 04 Sep 1993

IT **3380-34-5**, Triclosan
RL: BIOL (Biological study)
(antimicrobial topical compns. containing polyacrylamide and)

RN 3380-34-5 HCAPLUS

CN Phenol, 5-chloro-2-(2,4-dichlorophenoxy)- (7CI, 8CI, 9CI) (CA INDEX NAME)



IC ICM A61K047-32
ICS A61K007-48

CC 63-6 (Pharmaceuticals)

IT Anesthetics
Anti-infective agents
Antiarrhythmics
Antidepressants
Antiemetics
Antihistaminics
Antihypertensives
Antimalarials
Antitussives
Appetite depressants
Cardiotonics
Cholinergic agonists
Diuretics
Hypnotics and Sedatives
Inflammation inhibitors
Muscle relaxants
Neoplasm inhibitors
Nervous system stimulants
Sunscreens
Tranquilizers and Neuroleptics
Ulcer inhibitors
Vasoconstrictors
Vasodilators
Wound healing promoters
(topical compns. containing polyacrylamide and)

IT 55-56-1, Chlorhexidine 57-62-5, Chlortetracycline 57-92-1, Streptomycin, biological studies 59-01-8, Kanamycin 74-55-5, Ethambutol 79-57-2, Oxytetracycline 100-33-4, Pentamidine 100-97-0, biological studies 154-21-2 443-48-1, Metronidazole 564-25-0 768-94-5, Tricyclo[3.3.1.13,7]decan-1-amine 914-00-1, Methacycline

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FILE 'REGISTRY' ENTERED AT 09:39:29 ON 14 DEC 2004
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STRUCTURE FILE UPDATES: 13 DEC 2004 HIGHEST RN 796963-46-7
DICTIONARY FILE UPDATES: 13 DEC 2004 HIGHEST RN 796963-46-7

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> fil hcap

FILE 'HCAPLUS' ENTERED AT 09:39:31 ON 14 DEC 2004
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FILE COVERS 1907 - 14 Dec 2004 VOL 141 ISS 25
FILE LAST UPDATED: 13 Dec 2004 (20041213/ED)

This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> file stnguide

FILE 'STNGUIDE' ENTERED AT 09:39:33 ON 14 DEC 2004
USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Dec 10, 2004 (20041210/UP).

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=>

=> => d que l31
L4            44 SEA FILE=REGISTRY ABB=ON  PLU=ON  3380-34-5/RN,CRN
L5             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  17397-89-6/RN,CRN
L6          2143 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L4
L7           421 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L5
L16           34 SEA FILE=HCAPLUS ABB=ON  PLU=ON  101-84-8D? (L) ?HYDROXY?
L17            1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L16 AND ?MALARI?
L18           10 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L16 AND L6
L19            0 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L16 AND L7
L20           10 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L17 OR L18 OR L19)
L21        26898 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ?MALARI? OR ?PLASMOD?
L22       302260 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ?FATTY ACID?
L23       348360 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "FATTY ACIDS"+PFT,NT/CT
L24       102974 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "FATTY ACIDS, BIOLOGICAL
                 STUDIES"+PFT,NT/CT
L25         2675 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "FATTY ACID SYNTHETASE"+PFT,NT
                 /CT
L26            0 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "FATTY ACID SYNTHESIS"+PFT,NT/
                 CT
L27            0 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "FATTY ACID SYNTHASE"+PFT,NT/C
                 T
L28            1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L16 AND L21
L29            2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L16 AND (L22 OR L23 OR L24 OR
                 L25 OR L26 OR L27)
L30            2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L16 AND ((L22 OR L23 OR L24
                 OR L25 OR L26 OR L27))
L31           10 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L20 OR (L28 OR L29 OR L30)


=> d ibib abs ed l31
YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS' - CONTINUE? (Y)/N:y


L31 ANSWER 1 OF 10  HCAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:         2002:946029  HCAPLUS
DOCUMENT NUMBER:          138:8267
TITLE:                    Clear colorless solutions of alkoxylated alkanol amide
                          surfactants and antimicrobial compounds
INVENTOR(S):              Gormley, John L.; Reilly, James E.
PATENT ASSIGNEE(S):       ICI Americas Inc., USA
SOURCE:                   PCT Int. Appl., 24 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE         APPLICATION NO.          DATE
     ---------------      ----   --------     --------------------     --------
     WO 2002098222         A1    20021212     WO 2002-US17824          20020530
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
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CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003091667	A1	20030515	US 2002-161447	20020530
BR 2002005513	A	20030624	BR 2002-5513	20020530
EP 1392116	A1	20040303	EP 2002-739702	20020530
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004535416	T2	20041125	JP 2003-501274	20020530

PRIORITY APPLN. INFO.: US 2001-294587P P 20010601
WO 2002-US17824 W 20020530

OTHER SOURCE(S): MARPAT 138:8267

AB A visually clear and substantially colorless solution comprises (a) an antimicrobial compound selected from the group consisting of tea tree oil and a halogenated hydroxydiphenyl ether and (b) at least 20 weight percent, relative to the total weight of the solution, of at least one alkoxylated alkanolamide surfactant R1C(:O)N(H)CH2CH(R2)O[CH2CH(R2)O]xH (R1 = hydrocarbyl; R2 = H, C1-C6 hydrocarbyl, or a mixture thereof; x average > 0.2), said solution having a Gardner Color Value (GSV) below 8. The antimicrobial-containing solns. are suitable for readily mixing into cosmetics and disinfectant cleaning products.

ED Entered STN: 13 Dec 2002

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d l31 hitind
YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS' - CONTINUE? (Y)/N:y

L31 ANSWER 1 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN

IC ICM A01N025-30
ICS A01N031-16; A61K007-50; A61K031-085; A61K031-16; C11D017-08

CC 62-4 (Essential Oils and Cosmetics)
Section cross-reference(s): 1, 5, 63

IT **3380-34-5**, Triclosan
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Oletron; clear colorless solns. of alkoxylated alkanol amide surfactants and antimicrobial compds.)

IT **101-84-8D**, Diphenyl ether, **hydroxy**, halogenated
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(clear colorless solns. of alkoxylated alkanol amide surfactants and antimicrobial compds.)

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YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS' - CONTINUE? (Y)/N:y

YOU HAVE REQUESTED DATA FROM 9 ANSWERS - CONTINUE? Y/(N):y

L31 ANSWER 2 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:555566 HCAPLUS
DOCUMENT NUMBER: 137:110028
TITLE: Amorphous, antimicrobial, transparent film consisting of a thermoplastic that can be crystallized, method for the production and use thereof
INVENTOR(S): Murschall, Ursula; Kern, Ulrich; Crass, Guenther

PATENT ASSIGNEE(S): Mitsubishi Polyester Film G.m.b.H., Germany
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002057349	A1	20020725	WO 2002-EP85	20020108
W: JP, KR, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
DE 10101902	A1	20020718	DE 2001-10101902	20010117
DE 10101903	A1	20020926	DE 2001-10101903	20010117

PRIORITY APPLN. INFO.: DE 2001-10101902 A 20010117
DE 2001-10101903 A 20010117

AB The invention relates to an amorphous, antimicrobial, transparent film consisting of a thermoplastic that can be crystallized (such as polyesters), whose thickness ranges between 30 and 1000 μm. Said film contains the thermoplastic as the main component and in addition 2,4,4'-trichloro-2'-hydroxydiphenyl ether (Triclosan) as the antimicrobial component, either on its own or as part of a mixture with other antimicrobial substances. The film is characterized by cost-effective thermoforming properties, excellent optical characteristics and by an antimicrobial action. It can also exhibit UV stability, resistance to discoloration, photo-oxidative stability and flame-retardant properties and may be heat-sealable. The invention also relates to a method for producing said film using masterbatch technol. whereby masterbatches of Triclosan and the thermoplastic are used and to the use thereof.

ED Entered STN: 26 Jul 2002
IC ICM C08K005-00
ICS C08J005-18; B32B027-00; A01N031-08; A01N031-16
CC 37-6 (Plastics Manufacture and Processing)
IT 56-35-9, Tributyltin oxide 58-36-6, 10,10'-Oxybisphenoxarsine **101-84-8D**, Diphenyl ether, halogenated 5035-58-5, Diphenylantimony 2-ethylhexanoate 10380-28-6, Copper 8-hydroxyquinoline
RL: MOA (Modifier or additive use); USES (Uses)
(addnl. microbicide; amorphous, antimicrobial, transparent film containing crystallizable polyesters and **trichlorohydroxydiphenyl** ether)
IT **3380-34-5**, Triclosan
RL: MOA (Modifier or additive use); USES (Uses)
(amorphous, antimicrobial, transparent film containing crystallizable polyesters and trichlorohydroxydiphenyl ether)
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 3 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:555565 HCAPLUS
DOCUMENT NUMBER: 137:110027
TITLE: Amorphous, pigmented, antimicrobial films based on crystallizable polyesters and their manufacture and use
INVENTOR(S): Murschall, Ursula; Kern, Ulrich; Crass, Guenther
PATENT ASSIGNEE(S): Mitsubishi Polyester Film G.m.b.H., Germany
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German

FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002057348	A2	20020725	WO 2002-EP84	20020108
WO 2002057348	A3	20021010		
W: JP, KR, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
DE 10101904	A1	20020718	DE 2001-10101904	20010117
DE 10101906	A1	20020926	DE 2001-10101906	20010117
PRIORITY APPLN. INFO.:			DE 2001-10101904 A	20010117
			DE 2001-10101906 A	20010117

AB The microbe resistance of amorphous, pigmented, 30-1000-μm films based on crystallizable polyesters is improved by addition of Triclosan (2,4,4'-trichloro-2'-hydroxydiphenyl ether) and, optionally, other microbicides to the pigmented, film-forming compns.
ED Entered STN: 26 Jul 2002
IC ICM C08K005-00
CC 37-6 (Plastics Manufacture and Processing)
Section cross-reference(s): 5
IT 56-35-9, Tributyltin oxide 58-36-6, 10,10'-Oxybisphenoxarsine **101-84-8D**, Diphenyl ether, halogenated 5035-58-5, Diphenylantimony 2-ethylhexanoate 10380-28-6, Copper 8-hydroxyquinoline
RL: MOA (Modifier or additive use); USES (Uses)
(addnl. microbicide; amorphous, pigmented, antimicrobial films based on crystallizable polyesters containing **trichlorohydroxydiphenyl** ether)
IT 1317-70-0, Anatase 1317-80-2, Rutile 1345-16-0, C.I. Pigment Blue 28 **3380-34-5**, Triclosan 7727-43-7, Blanc Fixe XR-HX
RL: MOA (Modifier or additive use); USES (Uses)
(amorphous, pigmented, antimicrobial films based on crystallizable polyesters containing trichlorohydroxydiphenyl ether)

L31 ANSWER 4 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:231372 HCAPLUS
DOCUMENT NUMBER: 136:336425
TITLE: Potent inhibition of estrogen sulfotransferase by hydroxylated metabolites of polyhalogenated aromatic hydrocarbons reveals alternative mechanism for estrogenic activity of endocrine disrupters
AUTHOR(S): Kester, Monique H. A.; Bulduk, Sema; Van Toor, Hans; Tibboel, Dick; Meinl, Walter; Glatt, Hansruedi; Falany, Charles N.; Coughtrie, Michael W. H.; Schuur, A. Gerlienke; Brouwer, Abraham; Visser, Theo J.
CORPORATE SOURCE: Departments of Internal Medicine and Pediatric Surgery, Erasmus University Medical Center, Rotterdam, 3015 GJ, Neth.
SOURCE: Journal of Clinical Endocrinology and Metabolism (2002), 87(3), 1142-1150
CODEN: JCEMAZ; ISSN: 0021-972X
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Polyhalogenated aromatic hydrocarbons (PHAHs), such as polychlorinated dibenzo-p-dioxins and dibenzofurans, polybrominated diphenylethers, and bisphenol A derivs. are persistent environmental pollutants, which are capable of interfering with reproductive and endocrine function in birds, fish, reptiles, and mammals. PHAHs exert estrogenic effects that may be

mediated in part by their hydroxylated metabolites (PHAH-OHs), the mechanisms of which remain to be identified. PHAH-OHs show low affinity for the ER. Alternatively, they may exert their estrogenic effects by inhibiting E2 metabolism As sulfation of E2 by estrogen sulfotransferase (SULT1E1) is an important pathway for E2 inactivation, inhibition of SULT1E1 may lead to an increased bioavailability of estrogens in tissues expressing this enzyme. Therefore, we studied the possible inhibition of human SULT1E1 by hydroxylated PHAH metabolites and the sulfation of the different compds. by SULT1E1. We found marked inhibition of SULT1E1 by various PHAH-OHs, in particular by compds. with two adjacent halogen substituents around the hydroxyl group that were effective at (sub)nanomolar concns. Depending on the structure, the inhibition is primarily competitive or noncompetitive. Most PHAH-OHs are also sulfated by SULT1E1. We also investigated the inhibitory effects of the various PHAH-OHs on E2 sulfation by human liver cytosol and found that the effects were strongly correlated with their inhibitions of recombinant SULT1E1 (r = 0.922). Based on these results, we hypothesize that hydroxylated PHAHs exert their estrogenic effects at least in part by inhibiting SULT1E1-catalyzed E2 sulfation.

ED Entered STN: 27 Mar 2002

CC 4-3 (Toxicology)

IT 79-94-7, 3,3',5,5'-Tetrabromobisphenol A 79-95-8, 3,3',5,5'-Tetrachlorobisphenol A 80-05-7, 4,4'-Isopropylidenediphenol, biological studies **101-84-8D**, Diphenylether, bromo derivs., **hydroxy** metabolites 132-64-9D, Dibenzofuran, chloro derivs., hydroxy metabolites 262-12-4D, Dibenzo(p)dioxin, chloro derivs., hydroxy metabolites **3380-34-5**, 2-Hydroxy-2',4,4'-trichlorodiphenyl ether 74423-77-1, 2-Hydroxy-7,8-dichlorodibenzofuran 82019-03-2, 2-Hydroxy-1,3,7,8-tetrachlorodibenzo-p-dioxin 82019-04-3, 2-Hydroxy-3,7,8-trichlorodibenzo-p-dioxin 91370-78-4 97741-80-5, 2-Hydroxy-7,8-Dichlorodibenzo-p-dioxin 103124-63-6, 2-Hydroxy-6,7,8-trichlorodibenzofuran 123566-84-7, 3-Hydroxy-2,4,7,8-tetrachlorodibenzofuran 150975-86-3, 3-Hydroxy-2,6,7,8-tetrachlorodibenzofuran 166892-31-5, 3-Hydroxy-2,4,7,8,9-pentachlorodibenzofuran 213701-11-2, 2-Hydroxy-1,3,7,8-tetrachlorodibenzofuran 213701-12-3, 1-Hydroxy-2,4,7,8-tetrachlorodibenzofuran 213701-13-4, 4-Hydroxy-1,3,6,7-Tetrachlorodibenzofuran 218303-98-1 218303-99-2
RL: ADV (Adverse effect, including toxicity); PRP (Properties); BIOL (Biological study)
(potent inhibition of estrogen sulfotransferase by **hydroxylated** metabolites of polyhalogenated aromatic hydrocarbons reveals alternative mechanism for estrogenic activity of endocrine disrupters)

REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 5 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:220889 HCAPLUS
DOCUMENT NUMBER: 136:248990
TITLE: Process for treating fiber materials with aqueous compositions containing fiber-reactive cyclodextrin derivatives and antimicrobial agents
INVENTOR(S): Mao, Jianwen; Stehlin, Albert; Ochs, Dietmar; Eliu, Victor Paul
PATENT ASSIGNEE(S): Ciba Specialty Chemicals Holding Inc., Switz.
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002022941	A1	20020321	WO 2001-EP10283	20010906
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002013887	A5	20020326	AU 2002-13887	20010906
BR 2001013841	A	20030603	BR 2001-13841	20010906
EP 1319102	A1	20030618	EP 2001-982254	20010906
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: EP 2000-810825 A 20000914
EP 2001-810424 A 20010430
WO 2001-EP10283 W 20010906

OTHER SOURCE(S): MARPAT 136:248990

AB The process for antimicrobial treatment of fiber materials comprises applying to fiber materials (e.g., cotton fabric) with inclusion complexes of fiber-reactive cyclodextrin derivs. (e.g., Cavasol W 7MCT) and antimicrobial agents (e.g., 5-Chloro-2-(4-chlorophenoxy)phenol) selected from (a) halogeno-o-hydroxydiphenyl compds. or non-halogenated hydroxydiphenyl ether compds., (b) phenol derivs., (c) benzyl alcs., (d) chlorhexidine and its derivs., (e) C12-14 alkylbetaines and C8-C18 **fatty acid** Amidoalkylbetaines, (f) amphoteric surfactants, (g) trihalocarbanilides, (h) quaternary and polyquaternary compds. and (i) thiazole compds.

ED Entered STN: 22 Mar 2002

IC ICM D06M016-00
ICS D06M015-03

CC 40-9 (Textiles and Fibers)

IT 3380-30-1 **3380-34-5** 404834-79-3
RL: TEM (Technical or engineered material use); USES (Uses)
(antimicrobial agent; process for treating fiber materials with aqueous compns. containing fiber-reactive cyclodextrin derivs. and antimicrobial agents)

IT 55-56-1D, Chlorohexidine, derivs. 100-51-6D, Benzyl alcohol, derivs. **101-84-8D**, Diphenyl ether, (non)halogenated **hydroxy** derivs. 102-07-8D, Carbanilide, Trihalo derivs. 107-43-7D, Betaine, alkyl or **fatty acid** amidoalkyl derivs. 108-95-2D, Phenol, derivs. 288-47-1D, Thiazole, derivs.
RL: TEM (Technical or engineered material use); USES (Uses)
(antimicrobial agents; process for treating fiber materials with aqueous compns. containing fiber-reactive cyclodextrin derivs. and antimicrobial agents)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 6 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:12206 HCAPLUS
DOCUMENT NUMBER: 134:66128
TITLE: Use of hydroxydiphenyl ether class of chemicals, as exemplified by triclosan, as an **antimalarial** and identification of **fatty acid** synthesis as its target

INVENTOR(S): Namita, Surolina; Dharmarajan, Kamalapriya; Nagaraja, Thirumalapura Ramadhani
PATENT ASSIGNEE(S): Jawaharlal Nehru Centre for Advanced Scientific Research, India
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001000138	A2	20010104	WO 1999-IN26	19990623
WO 2001000138	A3	20020711		
WO 2001000138	B1	20021017		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9954424	A1	20010131	AU 1999-54424	19990623
BR 9913324	A	20010731	BR 1999-13324	19990623
EP 1137386	A2	20011004	EP 1999-940451	19990623
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: WO 1999-IN26 A 19990623

AB The use of hydroxydiphenyl ether class of chems., as exemplified by triclosan, (2,4,4'-trichloro-2'-hydroxydiphenyl ether), for both treatment and design of therapeutics for treatment of **malaria** is reported. More specifically, the present invention relates to identification of **fatty acid** synthesis as target for this compound as well as a key enzyme involved in synthesizing them. Inhibitory effects of triclosan on the growth of **Plasmodium** falciparum is shown. Mice infected with P. berghei were injected with 8., 14.0, and 28.0 mg triclosan/kg were survived while all the control group died by day 9 of infection.

ED Entered STN: 05 Jan 2001
IC ICM A61K
CC 1-5 (Pharmacology)
Section cross-reference(s): 61
ST hydroxydiphenyl ether **antimalarial fatty acid** synthesis; triclosan **antimalarial fatty acid** synthesis
IT Drug delivery systems
(injections, i.m.; use of hydroxydiphenyl ether class of chems. as **antimalarial** and identification of **fatty acid** synthesis as its target)
IT Drug delivery systems
(injections, i.p.; use of hydroxydiphenyl ether class of chems. as **antimalarial** and identification of **fatty acid** synthesis as its target)
IT **Antimalarials**
Plasmodium berghei
Plasmodium falciparum
(use of hydroxydiphenyl ether class of chems. as **antimalarial**

and identification of **fatty acid** synthesis as its target)

IT **Fatty acids, biological studies**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(use of hydroxydiphenyl ether class of chems. as **antimalarial** and identification of **fatty acid** synthesis as its target)

IT **101-84-8D**, Diphenyl ether, **hydroxy** derivs.
3380-34-5, Triclosan
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of **hydroxydiphenyl** ether class of chems. as **antimalarial** and identification of **fatty acid** synthesis as its target)

L31 ANSWER 7 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:283682 HCAPLUS
DOCUMENT NUMBER: 126:268543
TITLE: Biostatic coatings for medical devices containing halogenated hydroxy or acyloxy diphenyl ethers
INVENTOR(S): Fan, You Ling
PATENT ASSIGNEE(S): Union Carbide Chemicals and Plastics Company, Inc., USA
SOURCE: Eur. Pat. Appl., 12 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 761243	A1	19970312	EP 1996-306544	19960909
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CA 2185056	AA	19970309	CA 1996-2185056	19960909
BR 9603689	A	19980811	BR 1996-3689	19960909
PRIORITY APPLN. INFO.:			US 1995-3437P P	19950908

AB Hydrophilic, biostatic coatings suitable for coating medical devices are disclosed. The hydrophilic coatings comprise an antimicrobial agent selected from halogenated hydroxy or acyloxy di-Ph ethers. Surprisingly, the coatings exhibit excellent biostatic activities against many common infectious microorganisms even after prolonged durations. DMF 520, MEK 264, tert-Bu alc. 200, Myrj-53 0.5, poly(acrylic acid) 15 g were mixed and heated at 50° for 1 h, then cooled to room temperature and the product thus obtained was filtered to obtain a uniform colloidal dispersion. Then, 10.01 g of 2,4,4'-trichloro-2-hydroxydiphenyl ether was dissolved in 180.02 g of above dispersion and mixed to obtain the antimicrobial coating of the invention. Medical devices coated with above coating inhibited the growth of infectious bacteria.

ED Entered STN: 03 May 1997
IC ICM A61L029-00
ICS A61L031-00
CC 63-7 (Pharmaceuticals)
Section cross-reference(s): 38
IT **101-84-8D**, Diphenyl ether, derivs., halogenated **3380-34-5**, 2,4,4'-Tricholoro-2'-hydroxydiphenyl ether 9003-01-4, Poly(acrylic acid) 9004-34-6D, Cellulose, derivs., biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(biostatic coatings for medical devices containing halogenated **hydroxy** or acyloxy di-Ph ethers)

L31 ANSWER 8 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1994:708022 HCAPLUS
DOCUMENT NUMBER: 121:308022
TITLE: Oral hygiene pretreatment composition containing ethoxylated polymer
INVENTOR(S): Barnett, Paul; Burgon-lyon, Kirsty Helen; Cornwell, Emma Jane; Harbinson, Carys; Shaw, Michael Ian
PATENT ASSIGNEE(S): Smithkline Beecham PLC, UK
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9422417	A1	19941013	WO 1994-EP994	19940329
W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, LV, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9465375	A1	19941024	AU 1994-65375	19940329
PRIORITY APPLN. INFO.:			GB 1993-7005	A 19930402
			GB 1993-15531	A 19930727
			WO 1994-EP994	W 19940329

AB Oral hygiene compns. containing ≥1 polymer having pendant polyalkylene oxide groups are of use as a pretreatment step to enhance anti-plaque efficacy, prior to the use of an oral hygiene composition comprising an essentially water insol. noncationic antibacterial anti-plaque agent. Thus, bovine incisors pretreated in vitro with an aqueous solution of a methacrylic acid/methoxypolyethylene glycol methacrylate copolymer showed improved binding and retention of triclosan, an antibacterial agent.
ED Entered STN: 24 Dec 1994
IC ICM A61K007-16
CC 62-7 (Essential Oils and Cosmetics)
IT 65-85-0D, Benzoic acid, esters 101-81-5D, Diphenylmethane, halo hydroxy derivs. **101-84-8D**, Diphenyl ether, halo **hydroxy** derivs. 102-07-8D, derivs. 139-66-2D, Diphenyl thioether, halo hydroxy derivs. **3380-34-5**, Triclosan
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(oral hygiene pretreatment composition containing ethoxylated polymer)

L31 ANSWER 9 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1991:214200 HCAPLUS
DOCUMENT NUMBER: 114:214200
TITLE: Oral antiplaque compositions containing halo diphenyl ethers and their storage in compatible plastic container
PATENT ASSIGNEE(S): Colgate-Palmolive Co., USA
SOURCE: Neth. Appl., 41 pp.
CODEN: NAXXAN
DOCUMENT TYPE: Patent

LANGUAGE: Dutch
FAMILY ACC. NUM. COUNT: 15
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
NL 8903186	A	19900716	NL 1989-3186	19891229
US 4894220	A	19900116	US 1988-291712	19881229
US 5032386	A	19910716	US 1989-398566	19890825
US 5188821	A	19930223	US 1989-398592	19890825
US 5135738	A	19920804	US 1989-427660	19891026
SE 8904181	A	19910226	SE 1989-4181	19891212
SE 512333	C2	20000228		
AU 8946766	A1	19910228	AU 1989-46766	19891213
AU 640355	B2	19930826		
AU 8946771	A1	19910228	AU 1989-46771	19891213
AU 637777	B2	19930610		
IL 92694	A1	19940530	IL 1989-92694	19891213
GB 2235133	A1	19910227	GB 1989-28953	19891221
GB 2235133	B2	19940126		
GB 2235201	A1	19910227	GB 1989-28954	19891221
GB 2235201	B2	19940216		
GB 2257362	A1	19930113	GB 1992-16778	19891221
GB 2257362	B2	19930901		
GB 2263066	A1	19930714	GB 1993-5553	19891221
GB 2263066	B2	19930714		
IN 173759	A	19940709	IN 1989-DE1224	19891221
DE 3942641	A1	19910228	DE 1989-3942641	19891222
DE 3942641	C2	20020808		
DE 3942644	A1	19910228	DE 1989-3942644	19891222
CA 2006707	AA	19910225	CA 1989-2006707	19891227
CA 2006707	C	20010130		
CA 2006718	AA	19910225	CA 1989-2006718	19891227
CA 2006718	C	20001114		
CH 679674	A	19920331	CH 1989-4654	19891227
CH 680111	A	19920630	CH 1989-4655	19891227
DK 8906711	A	19910226	DK 1989-6711	19891228
DK 8906712	A	19910226	DK 1989-6712	19891228
NO 8905311	A	19910226	NO 1989-5311	19891228
NO 179161	B	19960513		
NO 179161	C	19960821		
FR 2651235	A1	19910301	FR 1989-17372	19891228
FR 2651124	A1	19910301	FR 1989-17374	19891228
FR 2651124	B1	19941104		
CN 1049606	A	19910306	CN 1989-109474	19891228
CN 1071110	B	20010919		
CN 1049669	A	19910306	CN 1989-109649	19891228
CN 1026005	B	19940928		
HU 54486	A2	19910328	HU 1989-6807	19891228
HU 210575	B	19950529		
ZA 8909970	A	19910828	ZA 1989-9970	19891228
ZA 8909973	A	19910925	ZA 1989-9973	19891228
ES 2023295	A6	19920101	ES 1989-4395	19891228
ES 2023297	A6	19920101	ES 1989-4397	19891228
CZ 281211	B6	19960717	CZ 1989-7511	19891228
RU 2066180	C1	19960910	RU 1989-4742780	19891228
FI 97443	B	19960913	FI 1989-6318	19891228
FI 97443	C	19961227		
CZ 283162	B6	19980114	CZ 1989-7509	19891228
CZ 283325	B6	19980218	CZ 1989-7512	19891228

SK 280834	B6	20000814	SK 1989-7509	19891228
BR 8906854	A	19901009	BR 1989-6854	19891229
NL 8903185	A	19910318	NL 1989-3185	19891229
NL 8903188	A	19910318	NL 1989-3188	19891229
DD 291244	A5	19910627	DD 1989-336812	19891229
BE 1004240	A4	19921020	BE 1989-1398	19891229
BE 1004366	A5	19921110	BE 1989-1396	19891229
PL 163551	B1	19940429	PL 1989-283116	19891229
PL 165411	B1	19941230	PL 1989-283119	19891229
JP 03083910	A2	19910409	JP 1990-213	19900104
JP 3112914	B2	20001127		
JP 03083911	A2	19910409	JP 1990-214	19900104
JP 2506473	B2	19960612		
IN 173866	A	19940730	IN 1990-DE119	19900212
IN 177709	A	19970215	IN 1991-DE1171	19911128
IN 178924	A	19970719	IN 1991-DE1169	19911128
IN 179787	A	19971206	IN 1991-DE1170	19911128
US 5279813	A	19940118	US 1992-931622	19920818
US 5292526	A	19940308	US 1992-966104	19921023
FR 2684550	A1	19930611	FR 1992-12748	19921026
FR 2684550	B1	19990122		
ZA 9303908	A	19950903	ZA 1993-3908	19930603
AU 9340058	A1	19931223	AU 1993-40058	19930604
AU 665422	B2	19960104		
BR 9302362	A	19940111	BR 1993-2362	19930615
EP 579383	A1	19940119	EP 1993-304646	19930615
EP 579383	B1	19970903		
R: AT, BE, CH, DE, DK, ES, FR, GB, IE, IT, LI, LU, NL, SE				
AT 157533	E	19970915	AT 1993-304646	19930615
RU 2116781	C1	19980810	RU 1993-29619	19930617
IN 180504	A	19980214	IN 1993-DE636	19930623
AU 9351999	A1	19940127	AU 1993-51999	19931126
AU 673014	B2	19961024		
US 5496540	A	19960305	US 1994-179272	19940110
US 5686064	A	19971111	US 1994-187984	19940128
SE 9703715	A	19971013	SE 1997-3715	19971013
SE 523627	C2	20040504		
SE 513702	C2	20001023	SE 1997-3714	19971013
PRIORITY APPLN. INFO.:			US 1988-291712 A	19881229
			US 1989-398566 A	19890825
			US 1989-398592 A	19890825
			US 1989-398605 A	19890825
			US 1989-398606 A	19890825
			US 1989-399669 A	19890825
			US 1989-410682 A	19890921
			US 1989-427660 A	19891026
			US 1987-8901 A2	19870130
			IN 1987-DE1148 A1	19871230
			US 1989-346258 A2	19890501
			GB 1989-28878 A	19891221
			GB 1989-28953 A3	19891221
			IN 1989-DE1223 A1	19891221
			US 1990-505628 A3	19900406
			US 1991-657885 A3	19910219
			US 1992-899412 A	19920616
			US 1992-931622 A3	19920818
			US 1992-966104 A3	19921023

AB An antiplaque antibacterial toothpaste, mouthwash, etc. containing as active agent a nearly water-insol. noncationic halogenated di-Ph ether is stored in a compatible plastic container made of e.g. poly(fluoroethylene) or

PVC. A stabilizer for the active agent, e.g. a terpene or essential oil, may also be present in the oral preparation Thus, a mouthwash contained deionized water 47.84, 70% aqueous sorbitol 20.00, 95% aqueous EtOH 12.50, glycerol 10.00, propylene glycol 7.00, 13% Gantrez S-97 solution 1.92, 50% aqueous NaOH 0.12, SDS 0.25, Tauranol WSHP 0.20, flavors containing ≥25% terpenes (of which ≥25% constituted limonene) 0.12, and triclosan (2',4,4'-trichloro-2-hydroxydiphenyl ether) 0.05%. The mouthwash was stored in PVC bottles at 41° for 3 or 5 wk; the loss of triclosan was <25% during this period.

ED Entered STN: 31 May 1991
IC ICM A61K007-16
CC 62-7 (Essential Oils and Cosmetics)
IT **3380-34-5**
RL: BIOL (Biological study)
(dentifrices containing, plastic containers compatible with)
IT **101-84-8D**, halo **hydroxy** derivs.
RL: BIOL (Biological study)
(plastic containers compatible with)

L31 ANSWER 10 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1986:620358 HCAPLUS
DOCUMENT NUMBER: 105:220358
TITLE: Thermotropic properties of human erythrocyte membrane proteins as affected by hydroxychloroaromatic compounds
AUTHOR(S): Miller, Terry L.; Smith, Robert J.
CORPORATE SOURCE: Environ. Health Sci. Cent., Oregon State Univ., Corvallis, OR, 97331, USA
SOURCE: Archives of Biochemistry and Biophysics (1986), 250(1), 128-38
CODEN: ABBIA4; ISSN: 0003-9861
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The thermal stability of the anion transport protein (band 3) and other proteins of the human erythrocyte membrane, as influenced by hydroxychloroarom. compds., was studied by SDC. Various hydroxychlorodiphenyl ethers (HCDPE) and hexachlorophene [70-30-4], but not pentachlorophenol [87-86-5], caused a marked decrease in the thermal stability of band 3. Most of the other calorimetric transitions of the erythrocyte membrane were only slightly affected. The activity of (HCDPE) toward lowering the transition temperature of band 3 generally increased with the degree of chlorination, and was somewhat dependent on the position of OH substitution. At higher concns. of HCDPE, there was a decrease in the enthalpy change and a broadening of the endothermic transition of band 3. The order of effectiveness of these compds., as determined from band 3 denaturation temps., was similar to the order of potency previously observed for hemolysis of human erythrocytes.

ED Entered STN: 26 Dec 1986
CC 4-3 (Toxicology)
IT **101-84-8D**, **chlorohydroxy** derivs. **3380-34-5**
21567-21-5 35245-80-8 42255-14-1 61639-90-5 78576-68-8
78576-70-2 78576-71-3 78576-72-4
RL: BIOL (Biological study)
(band 3 proteins thermal stability of human erythrocytes cell membrane response to)

=>
=>

=> fil hcap

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FILE COVERS 1907 - 13 Dec 2004 VOL 141 ISS 25
FILE LAST UPDATED: 12 Dec 2004 (20041212/ED)

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=> fil medlin

FILE 'MEDLINE' ENTERED AT 13:46:07 ON 13 DEC 2004

FILE LAST UPDATED: 9 DEC 2004 (20041209/UP). FILE COVERS 1950 TO DATE.

On February 29, 2004, the 2004 MeSH terms were loaded. See HELP RLOAD for details.

OLDMEDLINE now back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2004 vocabulary. See http://www.nlm.nih.gov/mesh/ and http://www.nlm.nih.gov/pubs/techbull/nd03/nd03_mesh.html for a description of changes.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> fil biosis

FILE 'BIOSIS' ENTERED AT 13:46:11 ON 13 DEC 2004

FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 9 December 2004 (20041209/ED)

FILE RELOADED: 19 October 2003.

=> fil pascal

FILE 'PASCAL' ENTERED AT 13:46:14 ON 13 DEC 2004

FILE LAST UPDATED: 13 DEC 2004 <20041213/UP>
FILE COVERS 1977 TO DATE.

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=> fil caba

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FILE COVERS 1973 TO 3 Dec 2004 (20041203/ED)

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=> fil jicst

FILE 'JICST-EPLUS' ENTERED AT 13:46:22 ON 13 DEC 2004
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FILE COVERS 1985 TO 6 DEC 2004 (20041206/ED)

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=> fil confsci

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FILE COVERS 1973 TO 18 Nov 2004 (20041118/ED)

=> fil wpix

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FILE LAST UPDATED: 8 DEC 2004 <20041208/UP>
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=> fil biotechno

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FILE LAST UPDATED: 7 JAN 2004       <20040107/UP>
FILE COVERS 1980 TO 2003.

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>>>  DERWENT DRUG FILE (SUBSCRIBER)  <<<

>>>  FILE COVERS 1983 TO DATE  <<<
>>>  THESAURUS AVAILABLE IN /CT  <<<

>>>  A RECENT REVIEW OF PSYCHIATRIC DISEASE KEYWORDS USED
     IN DERWENT DRUG FILE HAS PROMPTED A REVISION BASED
     ON STANDARD TERMS USED IN DSM-IV (DIAGNOSTIC AND
     STATISTICAL MANUAL OF MENTAL DISORDERS - FOURTH
     EDITION).
     FOR FURTHER DETAILS:
http://thomsonderwent.com/derwenthome/support/userguides/lit_guide


=> file stnguide
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=> d que l9
L1             1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  WO 1999-IN00026/APPS
L3            36 SEA FILE=HCAPLUS ABB=ON  PLU=ON  SUROLIA, N?/AU
L4            23 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L3 AND (?MALARI? OR ?PLASMOD?)

L6            24 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L4 OR L1
L7             7 SEA FILE=HCAPLUS ABB=ON  PLU=ON  NAMITA, S?/AU
L8             1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L7 AND (?MALARI? OR ?PLASMOD?)

L9            24 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L6 OR L8


=> fil hcap

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FILE COVERS 1907 - 13 Dec 2004  VOL 141 ISS 25
FILE LAST UPDATED: 12 Dec 2004  (20041212/ED)

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=> s l9 not l82
L184           10 L9 NOT L82

=> file stnguide

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=>
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Remove some duplicates

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FILE 'STNGUIDE' ENTERED AT 13:47:43 ON 13 DEC 2004

=>
(FILE 'MEDLINE, BIOSIS, PASCAL, CABA, JICST-EPLUS, CONFSCI, WPIX,
BIOTECHDS, BIOTECHNO, DRUGU' ENTERED AT 13:31:21 ON 13 DEC 2004)

=> d que l180
L176         122 SEA SUROLIA, N?/AU
L177          45 SEA NAMITA, S?/AU
L178      147955 SEA ?MALARI? OR ?ANTIMALARI?
L179          81 SEA (L176 OR L177) AND L178
L180          32 DUP REM L179 (49 DUPLICATES REMOVED)


=> dup rem l184 l180

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PROCESSING COMPLETED FOR L180
L185          34 DUP REM L184 L180 (8 DUPLICATES REMOVED)
                 ANSWERS '1-10' FROM FILE HCAPLUS
                 ANSWERS '11-23' FROM FILE MEDLINE
                 ANSWERS '24-28' FROM FILE BIOSIS
                 ANSWERS '29-33' FROM FILE CABA
                 ANSWER '34' FROM FILE WPIX

=> => dup rem l181 l185

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FILE 'DRUGU' ENTERED AT 13:49:16 ON 13 DEC 2004

FILE 'CABA' ENTERED AT 13:49:16 ON 13 DEC 2004

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PROCESSING COMPLETED
L186 98 DUP R ES REMOVED)
ANSWE
ANSWE LUS
ANSWE LINE
ANSWE ASE
ANSWE SIS
ANSWE DS
ANSWE TECHNO
ANSWE GU
ANSWERS '94-98' FROM A

Error

=> d ibib abs l185

L185 ANSWER 1 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2003:986818 HCAPLUS
DOCUMENT NUMBER: 140:334589
TITLE: Crystallization and preliminary crystallographic analysis of β-hydroxyacyl ACP dehydratase (FabZ) from **Plasmodium** falciparum
AUTHOR(S): Mukhi, Pidugu Lakshmi Swarna; Sharma, Shailendra Kumar; Kapoor, Mili; **Surolia, Namita**; Surolia, Avadhesha; Suguna, Kaza
CORPORATE SOURCE: Molecular Biophysics Unit, Indian Institute of Science, Bangalore, India
SOURCE: Acta Crystallographica, Section D: Biological Crystallography (2004), D60(1), 120-121
CODEN: ABCRE6; ISSN: 0907-4449
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The **malarial** parasite **Plasmodium** falciparum synthesizes fatty acids by the type II mechanism. In this cycle, the dehydration of β-hydroxyacyl acyl carrier protein ([ACP]) is catalyzed by β-Hydroxyacyl-[ACP] dehydratase (FabZ). Here, purified FabZ was crystallized using the hanging-drop vapor-diffusion and microbatch techniques. The crystals were orthorhombic, with space group I222 or I212121 and unit-cell parameters a = 71.78, b = 81.99, c = 97.49 Å. A complete data set to a resolution of 2.5 Å was collected under cryo-conditions (100 K) using a MAR imaging-plate detector system mounted on a rotating-anode x-ray generator.
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ibib abs l185 2-
YOU HAVE REQUESTED DATA FROM 33 ANSWERS - CONTINUE? Y/(N):y

L185 ANSWER 2 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 2003:212323 HCAPLUS

DOCUMENT NUMBER: 139:113568
TITLE: Functional characterization of β-ketoacyl-ACP reductase (FabG) from **Plasmodium** falciparum
AUTHOR(S): Pillai, Smitha; Rajagopal, Chitra; Kapoor, Mili; Kumar, Gyanendra; Gupta, Aditi; **Surolia, Namita**
CORPORATE SOURCE: Molecular Biology and Genetics Unit, Jawaharlal Nehru Centre for Advanced Scientific Research, Bangalore, Jakkur, 560064, India
SOURCE: Biochemical and Biophysical Research Communications (2003), 303(1), 387-392
CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Elsevier Science
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The **malaria** parasite, **Plasmodium** falciparum, unlike its human host, utilizes type II fatty acid synthesis, in which steps of fatty acid biosynthesis are catalyzed by independent enzymes. Due to this difference, the enzymes of this pathway are a potential target of newer **antimalarials.** Here we report the functional characterization of **Plasmodium** FabG expressed in Escherichia coli. The purified recombinant FabG from P. falciparum is soluble and active. The Km of the enzyme for acetoacetyl-CoA was estimated to be 75 μM with a Vmax of 0.0054 μmol/min/mL and a kcat value of 0.014 s-1. NADPH exhibited neg. cooperativity for its interaction with FabG. We have also modeled P. falciparum FabG using Brassica napus FabG as the template. This model provides a structural rationale for the specificity of FabG towards its cofactor, NADPH.
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L185 ANSWER 3 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 2002:863919 HCAPLUS
DOCUMENT NUMBER: 138:133539
TITLE: Survival strategies of the **malarial** parasite **Plasmodium** falciparum
AUTHOR(S): Ramya, T. N. C.; **Surolia, Namita**; Surolia, Avadhesha
CORPORATE SOURCE: Molecular Biophysics Unit, Indian Institute of Science, Bangalore, 560 012, India
SOURCE: Current Science (2002), 83(7), 818-825
CODEN: CUSCAM; ISSN: 0011-3891
PUBLISHER: Current Science Association
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review on several survival strategies adopted by the asexual blood stages of P. falciparum, including transport of macromols. and ions across the red blood cell into the parasite providing access to host nutrients; Hb digestion and heme detoxification; and novel metabolic pathways, especially those of the organelle apicoplast, as **antimalarial** targets.
REFERENCE COUNT: 85 THERE ARE 85 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L185 ANSWER 4 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 4
ACCESSION NUMBER: 2000:717930 HCAPLUS
DOCUMENT NUMBER: 134:25135
TITLE: Interaction of Chloroquine and Its Analogues with Heme: An Isothermal Titration Calorimetric Study
AUTHOR(S): Bachhawat, Kiran; Thomas, Celestine J.; **Surolia, Namita**; Surolia, Avadhesha

CORPORATE SOURCE: Molecular Biophysics Unit, Indian Institute of Science, Bangalore, 560012, India
SOURCE: Biochemical and Biophysical Research Communications (2000), 276(3), 1075-1079
CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Quinoline-containing drugs such as chloroquine and quinine have had a long and successful history in **antimalarial** chemotherapy. Identification of ferriprotoporphyrin IX ([Fe(III)PPIX], hematin) as the drug receptors for these **antimalarials** called for investigations of the binding affinity, mode of interaction, and the conditions affecting the interaction. The parameters obtained are significant in recent times with the emergence of chloroquine resistant strains of the **malaria** parasites. This has underlined the need to unravel the mol. mechanism of their action so as to meet the requirement of an alternative to the existing **antimalarial** drugs. The isothermal titration calorimetric studies on the interaction of chloroquine with hematin lead us to propose an altered mode of binding. The initial recognition is ionic in nature mediated by the propionyl group of hematin with the quaternary nitrogen on CQ. This ionic interaction induces a conformational change, such as to favor binding of subsequent CQ mols. On the contrary, conditions emulating the cytosolic environment (pH 7.4 and 150 mM salt) reveal the hydrophobic force to be the sole contributor driving the interaction. Interaction of a carefully selected panel of quinoline **antimalarial** drugs with monomeric ferriprotoporphyrin IX has also been investigated at pH 5.6 mimicking the acidic environment prevalent in the food vacuoles of parasite, the center of drug activity, which are consistent with their **antimalarial** activity. (c) 2000 Academic Press.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L185 ANSWER 5 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 5
ACCESSION NUMBER: 2000:141927 HCAPLUS
DOCUMENT NUMBER: 132:329255
TITLE: Receptor-mediated targeting of toxins to intraerythrocytic parasite **Plasmodium** falciparum
AUTHOR(S): **Surolia, N.**
CORPORATE SOURCE: Molecular Biology and Genetics Unit, Jawaharlal Nehru Centre for Advanced Scientific Research, Jakkur, Bangalore, India
SOURCE: Advanced Drug Delivery Reviews (2000), 41(2), 163-170
CODEN: ADDREP; ISSN: 0169-409X
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 48 refs. The increasing prevalence of drug-resistant **Plasmodium** falciparum **malaria** and the absence of effective vaccines or of vector control measures makes the development of new **antimalarial** drugs and other approaches for treating **malaria**, an urgent priority. The development of immunotoxins for targeted cytotoxic effects to kill the parasite is an attractive alternative therapeutic concept. The cytocidal effect of such hybrid mols. is highly specific and requires only minute doses. Cell surface receptor-directed targeting of toxins (hybrid toxins or immunotoxins) to human **malaria** parasite could eventually be developed as an effective therapy for **malaria.** Hybrid toxins may provide means

of controlling this dreadful disease and counter morbidity as well as mortality. Our results suggests that hybrid toxins are potent and efficacious in killing the parasite and that these agents should be examined in an appropriate in vivo model of **malaria.**

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L185 ANSWER 6 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 6
ACCESSION NUMBER: 2000:799553 HCAPLUS
DOCUMENT NUMBER: 134:83152
TITLE: Novel targets for **antimalarial** drug development
AUTHOR(S): **Surolia, Namita**
CORPORATE SOURCE: Molecular Biology and Genetics Unit, Jawaharlal Nehru Centre for Advanced Scientific Research, Bangalore, 560 064, India
SOURCE: Journal of the Indian Institute of Science (2000), 80(1), 17-23
CODEN: JIISAD; ISSN: 0019-4964
PUBLISHER: Indian Institute of Science
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 12 refs. Heme as well as protein biosynthetic pathways of **malaria** parasite **Plasmodium** falciparum have been identified as crucial for the survival of the parasite. Intervention of either of the two pathways results in the death of the parasite, basically due to the pivotal role played by heme in these pathways.
REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L185 ANSWER 7 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 7
ACCESSION NUMBER: 1996:663147 HCAPLUS
DOCUMENT NUMBER: 125:316311
TITLE: Cell surface receptor directed targeting of toxin to human **malaria** parasite, **Plasmodium** falciparum
AUTHOR(S): **Surolia, Namita**; Misquith, Sandra
CORPORATE SOURCE: Jawaharlal Nehru Centre for Advanced Scientific Research, Jakkur, Bangalore-560 064, India
SOURCE: FEBS Letters (1996), 396(1), 57-61
CODEN: FEBLAL; ISSN: 0014-5793
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Gelonin (a toxin and type II ribosome inactivating protein) when linked to human transferrin can be targeted to P. falciparum. The transferrin toxin conjugate is significantly toxic to parasite growth and is 25 times more potent than toxin alone in inhibiting parasite protein synthesis. The mechanism of its entry into the intraerythrocytic parasite is discussed.

L185 ANSWER 8 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 8
ACCESSION NUMBER: 1992:604631 HCAPLUS
DOCUMENT NUMBER: 117:204631
TITLE: De novo biosynthesis of heme offers a new chemotherapeutic target in the human **malarial** parasite
AUTHOR(S): **Surolia, Namita**; Padmanaban, Govindarajan
CORPORATE SOURCE: Dep. Biochem., Indian Inst. Sci., Bangalore, 560 012, India
SOURCE: Biochemical and Biophysical Research Communications

(1992), 187(2), 744-50
CODEN: BBRCA9; ISSN: 0006-291X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The human **malarial** parasite, **Plasmodium** falciparum, has been found to synthesize heme de novo, despite the accumulation of large quantities of polymeric heme derived from the Hb of the red cell host. The parasite δ-aminolevulinate dehydrase level is significantly lower than that of the host and its inhibition by succinylacetone leads to inhibition of parasite protein synthesis and viability.

L185 ANSWER 9 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:174278 HCAPLUS
DOCUMENT NUMBER: 133:99101
TITLE: Chloroquine binds in the cofactor binding site of **Plasmodium** falciparum lactate dehydrogenase - A response
AUTHOR(S): **Surolia, Namita**
CORPORATE SOURCE: Jawaharlal Nehru Centre for Advanced Scientific Research, Bungalore, 560064, India
SOURCE: Parasitology Today (2000), 16(3), 133
CODEN: PATOE2; ISSN: 0169-4758
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The crystal structure of the complex formed between chloroquine (CQ) and **Plasmodium** falciparum lactate dehydrogenase (PLDH) was discussed in terms of structure-based design of novel **antimalarials.** While it is important to analyze the complex of **antimalarial** CQ with PLDH, the use of these studies for developing **antimalarials** warrants caution, since PLDH is not found in the food vacuole of P. falciparum, which is the proposed site of action of CQ. QC exerts its effect on the food vacuole by forming a complex with heme that then either blocks the growing heme polymer of the enzymically or nonenzymically mediated formation of hemozoin. It appears that the CQ mode of action is through heme.

L185 ANSWER 10 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1991:484884 HCAPLUS
DOCUMENT NUMBER: 115:84884
TITLE: Chloroquine inhibits heme-dependent protein synthesis in **Plasmodium** falciparum
AUTHOR(S): **Surolia, Namita**; Padmanaban, Govindarajan
CORPORATE SOURCE: Dep. Biochem., Indian Inst. Sci., Bangalore, 560 012, India
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1991), 88(11), 4786-90
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A cell-free protein-synthesizing system has been reconstituted using the S-30 fraction or ribosomes and the S-100 fraction from P. falciparum. Addition of heme in vitro stimulates cell-free protein synthesis strikingly. Chloroquine inhibits the heme-dependent protein synthesis in the parasite lysate. The drug has also been found to inhibit parasite protein synthesis in situ at therapeutic concns. soon after addition to parasite cultures. Ribosomes as well as the S-100 fraction isolated from such chloroquine-treated cultures are defective in protein synthesis. Addition of hemin plus glucose 6-phosphate or high concns. of GTP, cAMP, and an active

preparation of eIF-2 to the parasite cell-free system restores protein synthesis to a significant extent in chloroquine-treated cultures. Under conditions of inhibition of protein synthesis in situ by chloroquine in the culture, the parasite eukaryotic initiation factor 2α-(eIF-2α) is phosphorylated in the parasite lysate to a greater extent than that observed in the control culture. Addition of hemin in vitro suppresses this phosphorylation. EIF-2α kinase activity is present in the parasite lysate and is not a contaminant derived from the human erythrocytes used to culture the parasite. The heme-chloroquine interactive effects can also be demonstrated with purified eIF-2α kinase from rabbit reticulocyte lysate. It is proposed that chloroquine inhibits heme-dependent protein synthesis in the parasite and this is an early event mediating the growth-inhibitory effects of the drug.

L185 ANSWER 11 OF 34 MEDLINE on STN
ACCESSION NUMBER: 2004367994 IN-PROCESS
DOCUMENT NUMBER: PubMed ID: 15139852
TITLE: Mutational analysis of the triclosan-binding region of enoyl-ACP (acyl-carrier protein) reductase from Plasmodium falciparum.
AUTHOR: Kapoor Mili; Gopalakrishnapai Jayashree; **Surolia Namita**; Surolia Avadhesha
CORPORATE SOURCE: Molecular Biophysics Unit, Indian Institute of Science, Bangalore-560012, India.
SOURCE: Biochemical journal, (2004 Aug 1) 381 (Pt 3) 735-41. Journal code: 2984726R. ISSN: 1470-8728.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20040725
Last Updated on STN: 20040728

AB Triclosan, a known antibacterial, acts by inhibiting enoyl-ACP (acyl-carrier protein) reductase (ENR), a key enzyme of the type II fatty acid synthesis (FAS) system. Plasmodium falciparum, the human **malaria**-causing parasite, harbours the type II FAS; in contrast, its human host utilizes type I FAS. Due to this striking difference, ENR has emerged as an important target for the development of new **antimalarials.** Modelling studies, and the crystal structure of P. falciparum ENR, have highlighted the features of ternary complex formation between the enzyme, triclosan and NAD+ [Suguna, A. Surolia and N. Surolia (2001) Biochem. Biophys. Res. Commun. 283, 224-228; Perozzo, Kuo, Sidhu, Valiyaveettil, Bittman, Jacobs, Fidock, and Sacchettini (2002) J. Biol. Chemical 277, 13106-13114; and Swarnamukhi, Kapoor, N. Surolia, A. Surolia and Suguna (2003) PDB1UH5]. To address the issue of the importance of the residues involved in strong specific and stoichiometric binding of triclosan to P. falciparum ENR, we mutated the following residues: Ala-217, Asn-218, Met-281, and Phe-368. The affinity of all the mutants was reduced for triclosan as compared with the wild-type enzyme to different extents. The most significant mutation was A217V, which led to a greater than 7000-fold decrease in the binding affinity for triclosan as compared with wild-type PfENR. A217G showed only 10-fold reduction in the binding affinity. Thus, these studies point out significant differences in the triclosan-binding region of the P. falciparum enzyme from those of its bacterial counterparts.

L185 ANSWER 12 OF 34 MEDLINE on STN
ACCESSION NUMBER: 2004367986 IN-PROCESS
DOCUMENT NUMBER: PubMed ID: 15125687
TITLE: Kinetic and structural analysis of the increased affinity

of enoyl-ACP (acyl-carrier protein) reductase for triclosan in the presence of NAD+.

AUTHOR: Kapoor Mili; Mukhi P L Swarna; **Surolia Namita**; Suguna K; Surolia Avadhesha

CORPORATE SOURCE: Molecular Biophysics Unit, Indian Institute of Science, Bangalore 560012, India.

SOURCE: Biochemical journal, (2004 Aug 1) 381 (Pt 3) 725-33. Journal code: 2984726R. ISSN: 1470-8728.

PUB. COUNTRY: England: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals

OTHER SOURCE: PDB-1UH5; PDB-1V35

ENTRY DATE: Entered STN: 20040725
Last Updated on STN: 20040728

AB The binding of enoyl-ACP (acyl-carrier protein) reductase from Plasmodium falciparum (PfENR) with its substrates and inhibitors has been analysed by SPR (surface plasmon resonance). The binding of the substrate analogue crotonoyl-CoA and coenzyme NADH to PfENR was monitored in real time by observing changes in response units. The binding constants determined for crotonoyl-CoA and NADH were 1.6x10(4) M(-1) and 1.9x10(4) M(-1) respectively. Triclosan, which has recently been demonstrated as a potent **antimalarial** agent, bound to the enzyme with a binding constant of 1.08x10(5) M(-1). However, there was a 300-fold increase in the binding constant in the presence of NAD+. The increase in the binding constant was due to a 17 times increase in the association rate constant (k(1)) from 741 M(-1) x s(-1) to 1.3x10(4) M(-1) x s(-1) and a 16 times decrease in the dissociation rate constant (k(-1)) from 6.84x10(-3) s(-1) to 4.2x10(-4) s(-1). These values are in agreement with those determined by steady-state kinetic analysis of the inhibition reaction [Kapoor, Reddy, Krishnasastry, N. Surolia and A. Surolia (2004) Biochem. J. 381, 719-724]. In SPR experiments, the binding of NAD+ to PfENR was not detected. However, a binding constant of 6.5x10(4) M(-1) was obtained in the presence of triclosan. Further support for these observations was provided by the crystal structures of the binary and ternary complexes of PfENR. Thus the dramatic enhancement in the binding affinity of both triclosan and NAD+ in the ternary complex can be explained by increased van der Waals contacts in the ternary complex, facilitated by the movement of residues 318-324 of the substrate-binding loop and the nicotinamide ring of NAD+. Interestingly, the results of the present study also provide a rationale for the increased affinity of NAD+ for the enzyme in the ternary complex.

L185 ANSWER 13 OF 34 MEDLINE on STN

ACCESSION NUMBER: 2004367963 IN-PROCESS

DOCUMENT NUMBER: PubMed ID: 15086316

TITLE: Slow-tight-binding inhibition of enoyl-acyl carrier protein reductase from Plasmodium falciparum by triclosan.

AUTHOR: Kapoor Mili; Reddy C Chandramouli; Krishnasastry M V; **Surolia Namita**; Surolia Avadhesha

CORPORATE SOURCE: Molecular Biophysics Unit, Indian Institute of Science, Bangalore-560012, India.

SOURCE: Biochemical journal, (2004 Aug 1) 381 (Pt 3) 719-24. Journal code: 2984726R. ISSN: 1470-8728.

PUB. COUNTRY: England: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals

ENTRY DATE: Entered STN: 20040725
Last Updated on STN: 20040728

AB Triclosan is a potent inhibitor of FabI (enoyl-ACP reductase, where ACP stands for acyl carrier protein), which catalyses the last step in a sequence of four reactions that is repeated many times with each elongation step in the type II fatty acid biosynthesis pathway. The **malarial** parasite Plasmodium falciparum also harbours the genes and is capable of synthesizing fatty acids by utilizing the enzymes of type II FAS (fatty acid synthase). The basic differences in the enzymes of type I FAS, present in humans, and type II FAS, present in Plasmodium, make the enzymes of this pathway a good target for **antimalarials**. The steady-state kinetics revealed time-dependent inhibition of FabI by triclosan, demonstrating that triclosan is a slow-tight-binding inhibitor of FabI. The inhibition followed a rapid equilibrium step to form a reversible enzyme-inhibitor complex (EI) that isomerizes to a second enzyme-inhibitor complex (EI*), which dissociates at a very slow rate. The rate constants for the isomerization of EI to EI* and the dissociation of EI* were 5.49x10(-2) and 1x10(-4) s(-1) respectively. The K(i) value for the formation of the EI complex was 53 nM and the overall inhibition constant K(i)* was 96 pM. The results match well with the rate constants derived independently from fluorescence analysis of the interaction of FabI and triclosan, as well as those obtained by surface plasmon resonance studies [Kapoor, Mukhi, N. Surolia, Sugunda and A. Surolia (2004) Biochem. J. 381, 725-733].

L185 ANSWER 14 OF 34 MEDLINE on STN
ACCESSION NUMBER: 2004530018 IN-PROCESS
DOCUMENT NUMBER: PubMed ID: 15315475
TITLE: 'FAS't inhibition of **malaria.**
AUTHOR: Surolia Avadhesha; Ramya T N C; Ramya V; **Surolia Namita**
CORPORATE SOURCE: Molecular Biophysics Unit, Indian Institute of Science, Bangalore 560012, India. surolia@mbu.iisc.ernet.in or. surolia@jncasr.ac.in
SOURCE: Biochemical journal, (2004 Nov 1) 383 (Pt. 3) 401-12. Journal code: 2984726R. ISSN: 1470-8728.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20041026
Last Updated on STN: 20041027

AB **Malaria**, a tropical disease caused by Plasmodium sp., has been haunting mankind for ages. Unsuccessful attempts to develop a vaccine, the emergence of resistance against the existing drugs and the increasing mortality rate all call for immediate strategies to treat it. Intense attempts are underway to develop potent analogues of the current **antimalarials**, as well as a search for novel drug targets in the parasite. The indispensability of apicoplast (plastid) to the survival of the parasite has attracted a lot of attention in the recent past. The present review describes the origin and the essentiality of this relict organelle to the parasite. We also show that among the apicoplast specific pathways, the fatty acid biosynthesis system is an attractive target, because its inhibition decimates the parasite swiftly unlike the 'delayed death' phenotype exhibited by the inhibition of the other apicoplast processes. As the enzymes of the fatty acid biosynthesis system are present as discrete entities, unlike those of the host, they are amenable to inhibition without impairing the operation of the host-specific pathway. The present review describes the role of these enzymes, the status of their molecular characterization and the current advancements in the area of developing inhibitors against each of the enzymes of the pathway.

L185 ANSWER 15 OF 34 MEDLINE on STN
ACCESSION NUMBER: 2003538429 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12930838
TITLE: Identification, characterization, and inhibition of Plasmodium falciparum beta-hydroxyacyl-acyl carrier protein dehydratase (FabZ).
AUTHOR: Sharma Shailendra Kumar; Kapoor Mili; Ramya T N C; Kumar Sanjay; Kumar Gyanendra; Modak Rahul; Sharma Shilpi; **Surolia Namita**; Surolia Avadhesha
CORPORATE SOURCE: Molecular Biophysics Unit, Indian Institute of Science, Bangalore 560012, India.
SOURCE: Journal of biological chemistry, (2003 Nov 14) 278 (46) 45661-71.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AY118082
ENTRY MONTH: 200312
ENTRY DATE: Entered STN: 20031119
Last Updated on STN: 20031225
Entered Medline: 20031224

AB The emergence of drug-resistant forms of Plasmodium falciparum emphasizes the need to develop new **antimalarials.** In this context, the fatty acid biosynthesis (FAS) pathway of the **malarial** parasite has recently received a lot of attention. Due to differences in the fatty acid biosynthesis systems of Plasmodium and man, this pathway is a good target for the development of new and selective therapeutic drugs directed against **malaria.** In continuation of these efforts we report cloning and overexpression of P. falciparum beta-hydroxyacyl-acyl carrier protein (ACP) dehydratase (PffabZ) gene that codes for a 17-kDa protein. The enzyme catalyzes the dehydration of beta-hydroxyacyl-ACP to trans-2-acyl-ACP, the third step in the elongation phase of the FAS cycle. It has a Km of 199 microM and kcat/Km of 80.4 m-1 s-1 for the substrate analog beta-hydroxybutyryl-CoA but utilizes crotonoyl-CoA, the product of the reaction, more efficiently (Km = 86 microM, kcat/Km = 220 m-1 s-1). More importantly, we also identify inhibitors (NAS-91 and NAS-21) for the enzyme. Both the inhibitors prevented the binding of crotonoyl-CoA to PfFabZ in a competitive fashion. Indeed these inhibitors compromised the growth of P. falciparum in cultures and inhibited the parasite fatty acid synthesis pathway both in cell-free extracts as well as in situ. We modeled the structure of PfFabZ using Escherichia coli beta-hydroxydecanoyl thioester dehydratase (EcFabA) as a template. We also modeled the inhibitor complexes of PfFabZ to elucidate the mode of binding of these compounds to FabZ. The discovery of the inhibitors of FabZ, reported for the first time against any member of this family of enzymes, essential to the type II FAS pathway opens up new avenues for treating a number of infectious diseases including **malaria.**

L185 ANSWER 16 OF 34 MEDLINE on STN
ACCESSION NUMBER: 2003538590 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14619956
TITLE: Triclosan: a shot in the arm for **antimalarial** chemotherapy.
AUTHOR: Rao Satish P Ramachandra; Surolia Avadhesha; **Surolia Namita**
CORPORATE SOURCE: Molecular Biophysics Unit, Indian Institute of Science, Bangalore, India.

SOURCE: Molecular and cellular biochemistry, (2003 Nov) 253 (1-2) 55-63. Ref: 98
Journal code: 0364456. ISSN: 0300-8177.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200409
ENTRY DATE: Entered STN: 20031119
Last Updated on STN: 20040917
Entered Medline: 20040916

AB In order that **malaria** be successfully contained, it is important that one has a clear understanding of the normal physiology and biochemistry of the parasite essential to its survival in its human host. Until very recently, the conventional approaches to **antimalarial** chemotherapy have consistently been plagued with the uncanny ability of the parasite to evolve resistance to drugs. The recently discovered plasmodial fatty acid biosynthetic pathway as well as its inhibition by triclosan that classifies it as belonging to type II, provide with a very crucial breakthrough to the crusade against **malaria.** How triclosan could tilt the balance in favor of the human hosts of the **malarial** parasite in a **malarial** condition is discussed.

L185 ANSWER 17 OF 34 MEDLINE on STN
ACCESSION NUMBER: 2002120845 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11835284
TITLE: Paradigm shifts in **malaria** parasite biochemistry and anti-**malarial** chemotherapy.
AUTHOR: **Surolia Namita**; RamachandraRao Satish P; Surolia Avadhesha
CORPORATE SOURCE: Molecular Biology and Genetics Unit, Jawaharlal Nehru Centre for Advanced Scientific Research, Jakkur, Bangalore 560 064, India.. surolia@mbu.iisc.ernet.in
SOURCE: BioEssays : news and reviews in molecular, cellular and developmental biology, (2002 Feb) 24 (2) 192-6.
Journal code: 8510851. ISSN: 0265-9247.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200207
ENTRY DATE: Entered STN: 20020222
Last Updated on STN: 20020702
Entered Medline: 20020701

AB A fatty acid synthesis (FAS) pathway was recently discovered and established in the obligate human parasite Plasmodium falciparum. Its inhibition by triclosan (2,4,4'-trichloro-2'-hydroxydiphenyl ether) leads to its classification as a type II FAS. Humans, the vertebrate host for the **malarial** parasite utilize type I FAS, which is not inhibited by triclosan. This discovery thus paves the way for novel approaches to the treatment of **malaria.** In direct contrast to the delayed-death phenotype associated with poisoning of the apicoplast using certain other drugs, the rapid and striking action of triclosan suggests the possibility of developing new drug(s) for the treatment of **malaria.**

L185 ANSWER 18 OF 34 MEDLINE on STN

ACCESSION NUMBER: 2002088915 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11735121
TITLE: Kinetic determinants of the interaction of enoyl-ACP reductase from Plasmodium falciparum with its substrates and inhibitors.
AUTHOR: Kapoor M; Dar M J; Surolia A; **Surolia N**
CORPORATE SOURCE: Molecular Biophysics Unit, Indian Institute of Science, Bangalore, India.
SOURCE: Biochemical and biophysical research communications, (2001 Dec 14) 289 (4) 832-7.
Journal code: 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200202
ENTRY DATE: Entered STN: 20020131
Last Updated on STN: 20020222
Entered Medline: 20020221

AB We have recently demonstrated that Plasmodium falciparum, unlike its human host, has the type II fatty acid synthase, in which steps of fatty acid biosynthesis are catalyzed by independent enzymes. This difference could be successfully exploited in the design of drugs specifically targeted at the different enzymes of this pathway in P. falciparum, without affecting the corresponding enzymes in humans. The importance of enoyl-ACP reductase (FabI) in the fatty acid biosynthesis pathway makes it an important target in **antimalarial** therapy. We report here the initial characterization of Plasmodium FabI expressed in Escherichia coli. The K(m) values of the enzyme for crotonyl-CoA and NADH were derived as 165 and 33 microM, respectively. Triclosan shows competitive kinetics with respect to NADH but is uncompetitive with respect to NAD(+), which shows that the binding of triclosan to the enzyme is facilitated in the presence of NAD(+).

L185 ANSWER 19 OF 34 MEDLINE on STN
ACCESSION NUMBER: 2001638389 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11693874
TITLE: In vitro **antimalarial** activity of extracts of three plants used in the traditional medicine of India.
AUTHOR: Bhat G P; **Surolia N**
CORPORATE SOURCE: Molecular Biology and Genetics Unit, Jawaharlal Nehru Center for Advanced Scientific Research, Bangalore, Karnataka State, India.
SOURCE: American journal of tropical medicine and hygiene, (2001 Oct) 65 (4) 304-8.
Journal code: 0370507. ISSN: 0002-9637.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 20011107
Last Updated on STN: 20020123
Entered Medline: 20011204

AB In an attempt to search for new **antimalarial** drugs, we studied plants used by traditional healers of southwest India to treat **malaria.** Aqueous and organic solvent extracts obtained from specific parts of the plants Swertia chirata, Carica papaya, and Citrus sinensis were tested on **malaria** strain Plasmodium falciparum FCK

2 in vitro. The temperatures of extraction were the same as that used by the traditional healers in their plant preparations. Visual evaluation of the **antimalarial** activity of the plant extracts on thin blood smears was followed by quantification of the activity by use of [35S]-methionine incorporation into parasite proteins to determine the value that inhibits 50% (IC50). Among the 3 plants tested, 2 had significant inhibitory effect on P. falciparum in vitro.

L185 ANSWER 20 OF 34 MEDLINE on STN
ACCESSION NUMBER: 2001262657 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11322792
TITLE: Structural basis for triclosan and NAD binding to enoyl-ACP reductase of Plasmodium falciparum.
AUTHOR: Suguna K; Surolia A; **Surolia N**
CORPORATE SOURCE: Molecular Biophysics Unit, Indian Institute of Science, Bangalore, 560 012, India.
SOURCE: Biochemical and biophysical research communications, (2001 Apr 27) 283 (1) 224-8.
Journal code: 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 20010521
Last Updated on STN: 20010521
Entered Medline: 20010517

AB Recent discovery of type II fatty acid synthase in the **malarial** parasite Plasmodium falciparum responsible for the most debilitating form of the disease in humans makes it ideal as a target for the development of novel **antimalarials.** Also, the identification of the enoyl-acyl carrier protein reductase from P. falciparum and the demonstration of its inhibition by triclosan [5-chloro-2-(2,4-dichlorophenoxy)phenol], a potent antibacterial compound, provide strong support for the above. In the studies reported here, a model of the enzyme in complex with triclosan and the cofactor NAD has been built by homology modeling with a view to understand its binding properties and to explore the potential of triclosan as a lead compound in designing effective **antimalarial** drugs. The model indeed provided the structural rationale for its interaction with ligands and the cofactor and revealed unique characteristics of its binding site which could be exploited for improving the specificity of the inhibitors.

L185 ANSWER 21 OF 34 MEDLINE on STN
ACCESSION NUMBER: 2001212640 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11175846
TITLE: Triclosan offers protection against blood stages of **malaria** by inhibiting enoyl-ACP reductase of Plasmodium falciparum.
COMMENT: Comment in: Nat Med 2001 Feb;7(2):149-50. PubMed ID: 11175835
Erratum in: Nat Med 2001 May;7(5)636
AUTHOR: **Surolia N**; Surolia A
CORPORATE SOURCE: Molecular Biology and Genetics Unit, Jawaharlal Nehru Centre for Advanced Scientific Research, Jakkur, Bangalore, India.
SOURCE: Nature medicine, (2001 Feb) 7 (2) 167-73.
Journal code: 9502015. ISSN: 1078-8956.
PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200104
ENTRY DATE: Entered STN: 20010425
Last Updated on STN: 20010425
Entered Medline: 20010419

AB The antimicrobial biocide triclosan [5-chloro-2-(2,4-dichlorophenoxy)phenol] potently inhibits the growth of Plasmodium falciparum in vitro and, in a mouse model, Plasmodium berghei in vivo. Inhibition of [14C]acetate and [14C]malonyl-CoA incorporation into fatty acids in vivo and in vitro, respectively, by triclosan implicate FabI as its target. Here we demonstrate that the enoyl-ACP reductase purified from P. falciparum is triclosan sensitive. Also, we present the evidence for the existence of FabI gene in P. falciparum. We establish the existence of the de novo fatty acid biosynthetic pathway in this parasite, and identify a key enzyme of this pathway for the development of new **antimalarials.**

L185 ANSWER 22 OF 34 MEDLINE on STN
ACCESSION NUMBER: 2001286713 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11255505
TITLE: Triclosan and fatty acid synthesis in Plasmodium falciparum: new weapon for an old enemy.
AUTHOR: Bhat G P; **Surolia N**
CORPORATE SOURCE: Molecular Biology and Genetics Unit, Jawaharlal Nehru Centre for Advanced Scientific Research, Jakkur, Bangalore 560 064, India.
SOURCE: Journal of biosciences, (2001 Mar) 26 (1) 1-3.
Journal code: 8100809. ISSN: 0250-5991.
PUB. COUNTRY: India
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 20010529
Last Updated on STN: 20010529
Entered Medline: 20010524

L185 ANSWER 23 OF 34 MEDLINE on STN
ACCESSION NUMBER: 94092131 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8267591
TITLE: Involvement of cytochrome P-450 in conferring chloroquine resistance to the **malarial** parasite, Plasmodium falciparum.
AUTHOR: **Surolia N**; Karthikeyan G; Padmanaban G
CORPORATE SOURCE: Department of Biochemistry, Indian Institute of Science, Bangalore.
SOURCE: Biochemical and biophysical research communications, (1993 Dec 15) 197 (2) 562-9.
Journal code: 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199401
ENTRY DATE: Entered STN: 19940209
Last Updated on STN: 19940209
Entered Medline: 19940125

AB The higher levels of cytochrome P-450 dependent enzyme activities reported

earlier are traced to higher levels of cytochrome P-450 (CYPIIB1/B2 like) messenger RNA in the chloroquine resistant than the sensitive strains. The messenger RNA is also induced by phenobarbitone in the sensitive strain. Pretreatment with phenobarbitone affords partial protection to chloroquine toxicity in the sensitive strain and this is not due to a differential accumulation of the drug.

L185 ANSWER 24 OF 34 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 2004:70156 BIOSIS
DOCUMENT NUMBER: PREV200400070737
TITLE: Fab end of a fascinating story of the development of novel anti-**malarials.**
AUTHOR(S): Surolia, A. [Reprint Author]; **Surolia, N.**
CORPORATE SOURCE: Indian Institute of Science, Bangalore, India
SOURCE: Molecular & Cellular Proteomics, (September 2003) Vol. 2, No. 9, pp. 992. print.
Meeting Info.: HUPO (Human Proteomics Organisation) 2nd Annual and IUBMB (International Union of Biochemistry and Molecular Biology) XIX World Congress. Montreal, Quebec, Canada. October 08-11, 2003. American Society for Biochemistry and Molecular Biology Inc.
ISSN: 1535-9476 (ISSN print).
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 4 Feb 2004
Last Updated on STN: 4 Feb 2004

L185 ANSWER 25 OF 34 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 2004:188818 BIOSIS
DOCUMENT NUMBER: PREV200400187028
TITLE: Plasmodium falciparum beta-hydroxyacyl-acyl carrier protein dehydratase (FabZ) as a potent **antimalarial** drug target.
AUTHOR(S): Sharma, Shailendra Kumar [Reprint Author]; Kapoor, Mili [Reprint Author]; Ramya, T. N. C. [Reprint Author]; Kumar, Sanjay; Kumar, Gyanendra [Reprint Author]; Modak, Rahul; Sharma, Shilpi [Reprint Author]; **Surolia, Namita**; Surolia, Avadhesha [Reprint Author]
CORPORATE SOURCE: Molecular Biophysics Unit, Indian Institute of Science, Bangalore, 560012, India
SOURCE: Medicinal Chemistry Research, (2003) Vol. 12, No. 6-7, pp. 371. print.
Meeting Info.: International Symposium on Current Trends in Drug Discovery Research. Lucknow, India. February 17-20, 2004.
ISSN: 1054-2523.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 7 Apr 2004
Last Updated on STN: 7 Apr 2004

L185 ANSWER 26 OF 34 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 2004:188568 BIOSIS
DOCUMENT NUMBER: PREV200400186939
TITLE: Exploring fatty acid synthesis in Plasmodium falciparum for

development of novel **antimalarials.**
AUTHOR(S): Surolia, A. [Reprint Author]; **Surolia, N.** [Reprint Author]
CORPORATE SOURCE: Jawaharlal Nehru Centre For Advanced Scientific Research, Indian Institute of Science, Bangalore, 560012, India
SOURCE: Medicinal Chemistry Research, (2003) Vol. 12, No. 4-5, pp. 169-170. print.
Meeting Info.: International Symposium on Current Trends in Drug Discovery Research. Lucknow, India. February 17-20, 2004.
ISSN: 1054-2523.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 7 Apr 2004
Last Updated on STN: 7 Apr 2004

L185 ANSWER 27 OF 34 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 2003:450794 BIOSIS
DOCUMENT NUMBER: PREV200300450794
TITLE: The Fab end of FAS and more.
AUTHOR(S): **Surolia, N.** [Reprint Author]
CORPORATE SOURCE: Jawaharlal Nehru Centre for Advanced Scientific Research, Jakkur, Bangalore, India
surolia@jncasr.ac.in
SOURCE: Bioscience Reports, (February 2003) Vol. 23, No. 1, pp. 25. print.
Meeting Info.: International Symposium on Modern Trends in Malaria. New Delhi, India. February 13-15, 2003.
ISSN: 0144-8463 (ISSN print).
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 1 Oct 2003
Last Updated on STN: 1 Oct 2003

L185 ANSWER 28 OF 34 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 2001:81012 BIOSIS
DOCUMENT NUMBER: PREV200100081012
TITLE: Heme: A key regulator in human **malaria** parasite Plasmodium falciparum.
AUTHOR(S): **Surolia, Namita** [Reprint author]
CORPORATE SOURCE: Molecular Biology and Genetics Unit, Jawaharlal Nehru Centre for Advanced Scientific Research, Bangalore, 64, India
SOURCE: Biochemical Society Transactions, (October, 2000) Vol. 28, No. 5, pp. A197. print.
Meeting Info.: 18th International Congress of Biochemistry and Molecular Biology. Birmingham, UK. July 16-20, 2000. International Union of Biochemistry and Molecular Biology; Federation of European Biochemical Societies; Biochemical Society.
CODEN: BCSTB5. ISSN: 0300-5127.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 14 Feb 2001
Last Updated on STN: 12 Feb 2002

L185 ANSWER 29 OF 34 CABA COPYRIGHT 2004 CABI on STN
ACCESSION NUMBER: 2004:159267 CABA
DOCUMENT NUMBER: 20043142319
TITLE: Mutational analysis of the triclosan-binding region of enoyl-ACP (acyl-carrier protein) reductase from Plasmodium falciparum
AUTHOR: Mili Kapoor; Jayashree Gopalakrishnapai; **Namita Surolia**; Avadhesha Surolia; Kapoor, M.; Gopalakrishnapai, J.; **Surolia, N.**; Surolia, A.
CORPORATE SOURCE: Molecular Biophysics Unit, Indian Institute of Science, Bangalore - 560 012, India. surolia@jncasr.ac.in
SOURCE: Biochemical Journal, (2004) Vol. 381, No. 3, pp. 735-741. 25 ref.
Publisher: Portland Press. Colchester
ISSN: 0264-6021
PUB. COUNTRY: United Kingdom
DOCUMENT TYPE: Journal
LANGUAGE: English
ENTRY DATE: Entered STN: 20041022
Last Updated on STN: 20041022

AB Triclosan, a known antibacterial, acts by inhibiting enoyl-ACP (acyl-carrier protein) reductase (ENR), a key enzyme of the type II fatty acid synthesis (FAS) system. Plasmodium falciparum, the human **malaria**-causing parasite, harbours the type II FAS; in contrast, its human host utilizes type I FAS. Due to this striking difference, ENR has emerged as an important target for the development of new **antimalarials.** Modelling studies, and the crystal structure of P. falciparum ENR, have highlighted the features of ternary complex formation between the enzyme, triclosan and NAD+ [Suguna, A. Surolia and N. Surolia (2001) Biochem. Biophys. Res. Commun. 283, 224-228; Perozzo, Kuo, Sidhu, Valiyaveettil, Bittman, Jacobs, Fidock, and Sacchettini (2002) J. Biol. Chemical 277, 13106-13114; and Swarnamukhi, Kapoor, N. Surolia, A. Surolia and Suguna (2003) PDB1UH5]. To address the issue of the importance of the residues involved in strong specific and stoichiometric binding of triclosan to P. falciparum ENR, we mutated the following residues: Ala-217, Asn-218, Met-281, and Phe-368. The affinity of all the mutants was reduced for triclosan as compared with the wild-type enzyme to different extents. The most significant mutation was A217V, which led to a greater than 7000-fold decrease in the binding affinity for triclosan as compared with wild-type PfENR. A217G showed only 10-fold reduction in the binding affinity. Thus, these studies point out significant differences in the triclosan-binding region of the P. falciparum enzyme from those of its bacterial counterparts.

L185 ANSWER 30 OF 34 CABA COPYRIGHT 2004 CABI on STN
ACCESSION NUMBER: 2004:159266 CABA
DOCUMENT NUMBER: 20043142318
TITLE: Kinetic and structural analysis of the increased affinity of enoyl-ACP (acyl-carrier protein) reductase for triclosan in the presence of NAD+
AUTHOR: Mili Kapoor; Mukhi, P. L. S.; **Namita Surolia** ; Suguna, K.; Avadhesha Surolia; Kapoor, M.; **Surolia, N.**; Surolia, A.
CORPORATE SOURCE: Molecular Biophysics Unit, Indian Institute of Science, Bangalore 560 012, India. surolia@jncasr.ac.in
SOURCE: Biochemical Journal, (2004) Vol. 381, No. 3, pp.

725-733. 42 ref.
Publisher: Portland Press. Colchester
ISSN: 0264-6021
PUB. COUNTRY: United Kingdom
DOCUMENT TYPE: Journal
LANGUAGE: English
ENTRY DATE: Entered STN: 20041022
Last Updated on STN: 20041022

AB The binding of enoyl-ACP (acyl-carrier protein) reductase from Plasmodium falciparum (PfENR) with its substrates and inhibitors has been analysed by SPR (surface plasmon resonance). The binding of the substrate analogue crotonoyl-CoA and coenzyme NADH to PfENR was monitored in real time by observing changes in response units. The binding constants determined for crotonoyl-CoA and NADH were 1.6x104 M-1 and 1.9x104 M-1 respectively. Triclosan, which has recently been demonstrated as a potent **antimalarial** agent, bound to the enzyme with a binding constant of 1.08x105 M-1. However, there was a 300-fold increase in the binding constant in the presence of NAD+. The increase in the binding constant was due to a 17 times increase in the association rate constant (k1) from 741 M-1 . s-1 to 1.3x104 M-1 . s-1 and a 16 times decrease in the dissociation rate constant (k-1) from 6.84x10-3 s-1 to 4.2x10-4 s-1. These values are in agreement with those determined by steady-state kinetic analysis of the inhibition reaction [Kapoor, Reddy, Krishnasastry, N. Surolia and A. Surolia (2004) Biochem. J. 381, 719-724]. In SPR experiments, the binding of NAD+ to PfENR was not detected. However, a binding constant of 6.5x104 M-1 was obtained in the presence of triclosan. Further support for these observations was provided by the crystal structures of the binary and ternary complexes of PfENR. Thus the dramatic enhancement in the binding affinity of both triclosan and NAD+ in the ternary complex can be explained by increased van der Waals contacts in the ternary complex, facilitated by the movement of residues 318-324 of the substrate-binding loop and the nicotinamide ring of NAD+. Interestingly, the results of the present study also provide a rationale for the increased affinity of NAD+ for the enzyme in the ternary complex.

L185 ANSWER 31 OF 34 CABA COPYRIGHT 2004 CABI on STN
ACCESSION NUMBER: 2004:159265 CABA
DOCUMENT NUMBER: 20043142317
TITLE: Slow-tight-binding inhibition of enoyl-acyl carrier protein reductase from Plasmodium falciparum by triclosan
AUTHOR: Mili Kapoor; Reddy, C. C.; Krishnasastry, M. V.; **Namita Surolia**; Avadhesha Surolia; Kapoor, M.; **Surolia, N.**; Surolia, A.
CORPORATE SOURCE: Molecular Biophysics Unit, Indian Institute of Science, Bangalore - 560 012, India. surolia@mbu.iisc.ernet.in
SOURCE: Biochemical Journal, (2004) Vol. 381, No. 3, pp. 719-724. 36 ref.
Publisher: Portland Press. Colchester
ISSN: 0264-6021
PUB. COUNTRY: United Kingdom
DOCUMENT TYPE: Journal
LANGUAGE: English
ENTRY DATE: Entered STN: 20041022
Last Updated on STN: 20041022

AB Triclosan is a potent inhibitor of FabI (enoyl-ACP reductase, where ACP stands for acyl carrier protein), which catalyses the last step in a sequence of four reactions that is repeated many times with each elongation step in the type II fatty acid biosynthesis pathway. The

malarial parasite Plasmodium falciparum also harbours the genes and is capable of synthesizing fatty acids by utilizing the enzymes of type II FAS (fatty acid synthase). The basic differences in the enzymes of type I FAS, present in humans, and type II FAS, present in Plasmodium, make the enzymes of this pathway a good target for **antimalarials**. The steady-state kinetics revealed time-dependent inhibition of FabI by triclosan, demonstrating that triclosan is a slow-tight-binding inhibitor of FabI. The inhibition followed a rapid equilibrium step to form a reversible enzyme-inhibitor complex (EI) that isomerizes to a second enzyme-inhibitor complex (EI*), which dissociates at a very slow rate. The rate constants for the isomerization of EI to EI* and the dissociation of EI* were 5.49x10-2 and 1x10-4 s-1 respectively. The Ki value for the formation of the EI complex was 53 nM and the overall inhibition constant Ki* was 96 pM. The results match well with the rate constants derived independently from fluorescence analysis of the interaction of FabI and triclosan, as well as those obtained by surface plasmon resonance studies.

L185 ANSWER 32 OF 34 CABA COPYRIGHT 2004 CABI on STN
ACCESSION NUMBER: 2000:80537 CABA
DOCUMENT NUMBER: 20000806540
TITLE: Chloroquine binds in the cofactor binding site of Plasmodium falciparum lactate dehydrogenase - a response
AUTHOR: **Namita Surolia; Surolia, N.;** Read, J. A.; Sessions, R. B.; Brady, R. L.
CORPORATE SOURCE: Jawaharlal Nehru Centre for Advanced Scientific Research, Jakkur Campus, Jakkur, PO Bangalore 560064, India.
SOURCE: Parasitology Today, (2000) Vol. 16, No. 3, pp. 133. 7 ref.
DOCUMENT TYPE: Letter
LANGUAGE: English
ENTRY DATE: Entered STN: 20000719
Last Updated on STN: 20000719

L185 ANSWER 33 OF 34 CABA COPYRIGHT 2004 CABI on STN
ACCESSION NUMBER: 97:24386 CABA
DOCUMENT NUMBER: 19970800928
TITLE: De novo biosynthesis of heme in Plasmodium falciparum
AUTHOR: **Namita Surolia; Surolia, N.**
CORPORATE SOURCE: Molecular Parasitology Laboratory, Jawaharlal Nehru Centre for Advanced Scientific Research, Jakkur, Bangalore 560 064, India.
SOURCE: Parasitology Today, (1996) Vol. 12, No. 12, pp. 495. 3 ref.
DOCUMENT TYPE: Letter
LANGUAGE: English
ENTRY DATE: Entered STN: 19970317
Last Updated on STN: 19970317
AB The correspondent comments on the statement by A.D. Sullivan and S.R. Meshnick (Parasitology Today (1996) 12, 161-163) that "...**malaria** parasites do have haem-containing proteins such as cytochromes, but no one has determined whether this haem is acquired or synthesized de novo" and refers to 2 papers which substantiated de novo haem biosynthesis in Plasmodium falciparum (Surolia, N.; Padmanaban, G., Biochemical and Biophysical Research Communications (1992) 187, 744-750, and Wilson, C. M., Molecular and Biochemical Parasitology (1996) 75, 271-276).

L185 ANSWER 34 OF 34 WPIX COPYRIGHT 2004 THE THOMSON CORP on STN

ACCESSION NUMBER: 2002-216205 [27] WPIX
DOC. NO. CPI: C2002-066075
TITLE: Use of hydroxydiphenyl ether class of chemicals e.g. triclosan for inhibiting growth of **malaria** parasite.
DERWENT CLASS: B05
INVENTOR(S): **SUROLIA, N**; SUROLIA, A
PATENT ASSIGNEE(S): (DHAR-I) DHARMARAJAN K; (JAWA-N) JAWAHARLAL NEHRU CENT ADVANCED SCI RES; (NAGA-I) NAGARAJA T R; (NAMI-I) NAMITA S; (JAWA-N) JAWAHARLAL CENT ADVANCED SCI RES; (SURO-I) SUROLIA N
COUNTRY COUNT: 87
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001000138	A2	20010104	(200227)*	EN	34
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW					
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW					
AU 9954424	A	20010131	(200227)		
BR 9913324	A	20010731	(200227)		
EP 1137386	A2	20011004	(200227)	EN	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
ZA 2001002305	A	20020626	(200270)#		39

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001000138	A2	WO 1999-IN26	19990623
AU 9954424	A	AU 1999-54424	19990623
		WO 1999-IN26	19990623
BR 9913324	A	BR 1999-13324	19990623
		WO 1999-IN26	19990623
EP 1137386	A2	EP 1999-940451	19990623
		WO 1999-IN26	19990623
ZA 2001002305	A	ZA 2001-2305	20010320

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9954424	A	Based on	WO 2001000138
BR 9913324	A	Based on	WO 2001000138
EP 1137386	A2	Based on	WO 2001000138

PRIORITY APPLN. INFO: WO 1999-IN26 19990623; ZA 2001-2305 20010320
AN 2002-216205 [27] WPIX
AB WO 200100138 A UPAB: 20021007
NOVELTY - Hydroxydiphenyl ether class of chemicals as exemplified by triclosan (2,4,4'-trichloro-2'-hydroxydiphenyl ether) (I) or their derivatives inhibit growth of **malaria** parasite by identification of fatty acid synthesis as its target.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(a) A composition comprising (I) or its derivative and an adjuvant, diluent or a carrier and is suitable for introduction into blood;

(b) A method of testing to confirm that the growth of human **malaria** parasite is inhibited by the use of (I) involves:

(1) examining smears of in vitro treated cultures for morphological features of the parasite as an indicator of growth; or

(2) monitoring the incorporation of (35S) methionine in protein as a quantitative indicator of the inhibition of the parasite growth;

(c) A method of determining the growth of animal **malaria** parasite inhibited by the use of (I) involves:

(1) monitoring the extent of inhibition of parasitemia by examining the smears of blood taken from an animal; or

(2) determining the reduction in the mortality rate of the treated mice vs. untreated mice;

(d) A method of determining the ability of any compound to inhibit the elongation in fatty acid synthesis in **malaria** parasite (preferably of human or animal origin), involves demonstrating the inhibition of fatty acid synthesis in the cell free fatty acid synthesis system of **malaria** parasite by estimating the amount of radioactively labeled malonyl-COA incorporated in fatty acids or analyzing the type of fatty acids synthesized by a chromatographic method;

(e) A method of inhibiting the elongation reaction of fatty acid synthesis in **malaria** parasite (preferably of human or animal origin) involves incubation of (I) with the parasite, cultures, animal models or in cell free systems derived from any kind of **malaria** parasite or any preparation containing the enzyme FabI of **malaria** parasite as the test system; and

(f) Any other class of compounds that inhibit the elongation of fatty acid synthesis in **malaria** parasite.

ACTIVITY - Protozoacide.

MECHANISM OF ACTION - Parasite growth inhibitor.

USE - To inhibit the growth of Plasmodium Falciparum (human **malaria** parasite) and P. berghei (animal e.g. mice parasite); and to inhibit the elongation in fatty acid synthesis in **malaria** parasite (all claimed).

Swiss male mice were infected with P. berghei. The animals were kept under observation and parasitemia was recorded daily. Triclosan (0.8, 1.6, 3, 8, 14 and 28 mg/kg body weight of mice respectively) in dimethylsulfoxide (DMSO) was given subcutaneously on day one of infection when parasitemia was greater than 1% and subsequently for the next 6 days. Experiments were conducted with a group of five animals, each for the above mentioned dosage. DMSO was given to 6 control animals and were referred to as untreated animals. Parasitemia and mortality were recorded till the untreated mice died. All of the mice in the control group died by day 9 of infection. Whilst 3 mice out of 5, 3 mice out of 5, and 4 mice out of 5 treated with 0.8, 1.6 and 3 mg of triclosan/kg survived till day 14. All the mice (5/5) survived till 14th day when

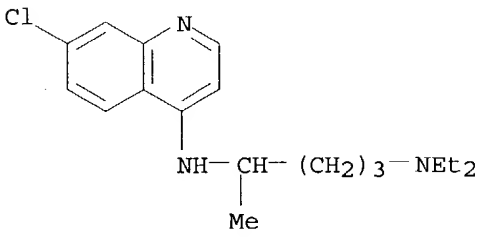
ADVANTAGE - The composition is suitable for introduction in the blood by any method.

Dwg.0/6

=>

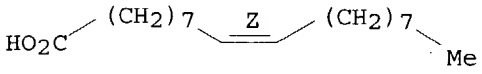
1403-66-3, Gentamicin 1404-04-2, Neomycin **3380-34-5**, Triclosan
7542-37-2, Paromomycin 10118-90-8, Minocycline 11003-38-6, Capreomycin
22916-47-8, Miconazole 32986-56-4, Tobramycin 37517-28-5, Amikacin
56391-56-1, Netilmicin 70458-96-7, Norfloxacin 85721-33-1, Ciprofloxacin
RL: BIOL (Biological study)
(antimicrobial topical compns. containing polyacrylamide and)

L181 ANSWER 19 OF 71 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1987:143846 HCAPLUS
DOCUMENT NUMBER: 106:143846
TITLE: Cytotoxicity of diphtheria toxin A fragment to toxin-resistant murine cells delivered by pH-sensitive immunoliposomes
AUTHOR(S): Collins, David; Huang, Leaf
CORPORATE SOURCE: Dep. Biochem., Univ. Tennessee, Knoxville, TN, 37996-0840, USA
SOURCE: Cancer Research (**1987**), 47(3), 735-9
CODEN: CNREA8; ISSN: 0008-5472
DOCUMENT TYPE: Journal
LANGUAGE: English
AB PH-sensitive immunoliposomes composed of dioleoylphosphatidylethanolamine [2462-63-7] and oleic acid [**112-80-1**] (8:2 molar ratio) mediated the delivery of the cytotoxic fragment A of diphtheria toxin to the cytoplasm of **target** L-929 cells. Free fragment A, fragment A encapsulated in antibody-free liposomes, or fragment A encapsulated in pH-insensitive immunolipsomes were not effective in the **inhibition** of the cellular protein **synthesis.** PH-sensitive immunoliposomes containing diphtheria fragment A were not toxic to **nontarget** diphtheria-resistant A31 cells or to **nontarget** diphtheria-sensitive Vero cells. Pretreatment of **target** L-929 cells with the weak bases(NH4Cl or chloroquine [**54-05-7**]), agents which raise the endosome/liposome pH, **blocked** the cytotoxic effect of the pH-sensitive immunoliposomes containing fragment A. Excess free antibody or excess empty pH-sensitive immunoliposomes also **blocked** the cytotoxic effect. Since it is known that fragment A alone cannot cross lipid membrnanes, the results indicate that pH-sensitive immunoliposomes are able to release the toxin into the cytoplasm, probably by fusing with the endosome membrane following receptor-mediated endocytosis of the immunoliposome.
ED Entered STN: 01 May 1987
IT **54-05-7**
RL: BIOL (Biological study)
(cytotoxicity of diphtheria toxin A fragment to resistant murine cells delivered by pH sensitive immunoliposomes in relation to)
RN 54-05-7 HCAPLUS
CN 1,4-Pentanediamine, N4-(7-chloro-4-quinolinyl)-N1,N1-diethyl- (9CI) (CA INDEX NAME)



IT **112-80-1**, biological studies
RL: BIOL (Biological study)
(immunoliposomes containing, pH-sensitive, cytotoxicity of diphtheria toxin A fragment to toxin resistant murine cells delivered by)
RN 112-80-1 HCAPLUS
CN 9-Octadecenoic acid (9Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



CC 63-3 (Pharmaceuticals)
IT **54-05-7** 12125-02-9, Ammonium chloride, uses and miscellaneous
RL: BIOL (Biological study)
(cytotoxicity of diphtheria toxin A fragment to resistant murine cells delivered by pH sensitive immunoliposomes in relation to)
IT **112-80-1**, biological studies 2462-63-7 68737-67-7, Dioleoylphosphatidylcholine
RL: BIOL (Biological study)
(immunoliposomes containing, pH-sensitive, cytotoxicity of diphtheria toxin A fragment to toxin resistant murine cells delivered by)

L181 ANSWER 20 OF 71 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1986:545885 HCAPLUS
DOCUMENT NUMBER: 105:145885
TITLE: Differential effects of mepacrine, chloroquine and hydroxychloroquine on superoxide anion generation, phospholipid methylation and arachidonic acid release by human blood monocytes
AUTHOR(S): Hurst, N. P.; French, J. K.; Bell, A. L.; Nuki, G.; O'Donnell, M. L.; Betts, W. H.; Cleland, L. G.
CORPORATE SOURCE: R. Adelaide Hosp., Queen Elizabeth Hosp., Woodville, 5011, Australia
SOURCE: Biochemical Pharmacology (**1986**), 35(18), 3083-9
CODEN: BCPCA6; ISSN: 0006-2952
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The 4-aminoquinolines chloroquine (CQ) [**54-05-7**] and hydroxychloroquine (HCQ) [118-42-3] and in the past the 9-aminoacridine mepacrine (MP) [83-89-6], have been widely used in the treatment of inflammatory disorders such as rheumatoid arthritis and systemic lupus erythematosus; the effects of these drugs on monocyte O21- **generation** elicited by 5 different stimuli (opsonised zymosan (STZ), FMLP, A23187, TPA and F-) were investigated and correlations were sought with effects on 2 processes which are linked with monocyte activation, namely arachidonic acid (AA) [**506-32-1**] release and transmethylation of phosphatidylethanolamine (PE) to phosphatidylcholine (PC). Neither CQ nor HCQ had any marked effect on O21- release induced by TPA, A23187 or F-, excluding an effect on type C protein kinase (PKC) [9026-43-1], calmodulin-dependent kinase [9031-44-1], or the membrane-bound, O21--**generating** NADP oxidase [9032-22-8]. In contrast, MP **inhibited** the response to TPA and A23187. Each drug also had different effects on surface receptor-dependent responses; thus HCQ **inhibited** FMLP- but not STZ-induced O21- release, whereas CQ and MP **inhibited** the response to both stimuli. Each drug also displayed different effects on AA release and phospholipid

(PL)-methylation; MP and HCQ, but not CQ, **inhibited** STZ-stimulated AA release while MP and CQ but not HCQ **inhibited** basal rates of PL-methylation in mononuclear cells. However, only MP **inhibited** PL-methylation in an enriched monocyte population. Thus, despite their close structural similarity, MP, CQ, and HCQ each have different metabolic effects and their actions cannot simply be attributed to **inhibition** of lysosomal functions. Other possible mechanisms of action are discussed. The selective effects of each drug also provide further evidence for multiple pathways of monocyte activation.

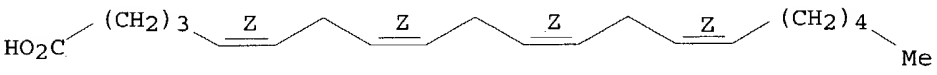
ED Entered STN: 01 Nov 1986

IT **506-32-1**
RL: BIOL (Biological study)
(release of, chloroquine and hydroxychloroquine and mepacrine effect on, in human monocyte)

RN 506-32-1 HCAPLUS

CN 5,8,11,14-Eicosatetraenoic acid, (5Z,8Z,11Z,14Z)- (9CI) (CA INDEX NAME)

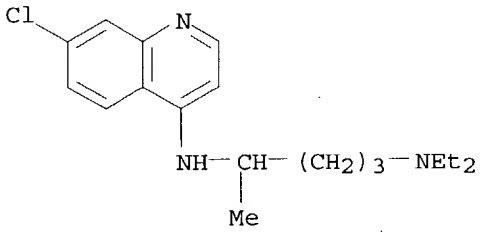
Double bond geometry as shown.



IT **54-05-7**
RL: BIOL (Biological study)
(superoxide formation and phospholipid methylation and arachidonic acid release by human monocyte response to)

RN 54-05-7 HCAPLUS

CN 1,4-Pentanediamine, N4-(7-chloro-4-quinolinyl)-N1,N1-diethyl- (9CI) (CA INDEX NAME)



CC 1-7 (Pharmacology)
Section cross-reference(s): 15

IT **506-32-1**
RL: BIOL (Biological study)
(release of, chloroquine and hydroxychloroquine and mepacrine effect on, in human monocyte)

IT **54-05-7** 83-89-6 118-42-3
RL: BIOL (Biological study)
(superoxide formation and phospholipid methylation and arachidonic acid release by human monocyte response to)

L181 ANSWER 21 OF 71 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1984:465447 HCAPLUS
DOCUMENT NUMBER: 101:65447
TITLE: Arachidonic acid cascade and anti-hypoxic drugs
AUTHOR(S): Nikolov, R.
CORPORATE SOURCE: Chem. Pharm. Res. Inst., Sofia, 1156, Bulg.

SOURCE: Methods and Findings in Experimental and Clinical Pharmacology (**1984**), 6(5), 231-4
CODEN: MFEPDX; ISSN: 0379-0355
DOCUMENT TYPE: Journal
LANGUAGE: English

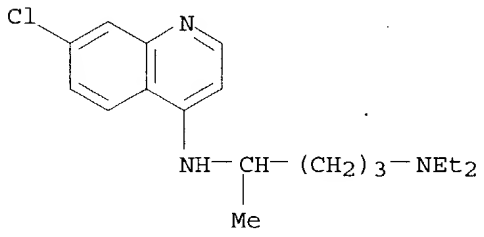
AB The antihypoxic effect of drugs that **inhibit** different steps of arachidonic acid **[506-32-1]** metabolism was studied using an exptl. model of acute hypobaric hypoxia in mice. The drugs investigated were chloroquine **[54-05-7]**, betamethasone [378-44-9], chlorpromazine [50-53-3] (phospholipase A2 **inhibitors**), ketoprofen [22071-15-4] (cyclooxygenase **inhibitor**), and imidazole [288-32-4] (TxA2 **synthetase inhibitor**). Prostacyclin [35121-78-9] and PGF2α [551-11-1] were also studied. All the **inhibitors** of arachidonic acid metabolism manifest an antihypoxic effect of a various degree. PGF2α had a deleterious effect, and PGI2 showed a marked antihypoxic effect. Thus, arachidonic acid cascade **inhibition** may serve as a useful model for screening antihypoxic agents.

ED Entered STN: 01 Sep 1984

IT **54-05-7**
RL: BIOL (Biological study)
(arachidonate metabolism response to, antihypoxic drug screen in relation to)

RN 54-05-7 HCAPLUS

CN 1,4-Pentanediamine, N4-(7-chloro-4-quinolinyl)-N1,N1-diethyl- (9CI) (CA INDEX NAME)

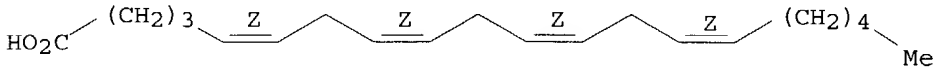


IT **506-32-1**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(metabolism of, inhibitors of, antihypoxic drug screening in relation to)

RN 506-32-1 HCAPLUS

CN 5,8,11,14-Eicosatetraenoic acid, (5Z,8Z,11Z,14Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



CC 1-1 (Pharmacology)
Section cross-reference(s): 2

IT 50-53-3, biological studies **54-05-7** 288-32-4, biological studies 378-44-9 551-11-1 22071-15-4 35121-78-9
RL: BIOL (Biological study)
(arachidonate metabolism response to, antihypoxic drug screen in relation to)

IT **506-32-1**

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(metabolism of, inhibitors of, antihypoxic drug screening in relation to)

L181 ANSWER 22 OF 71 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1980:489426 HCAPLUS
DOCUMENT NUMBER: 93:89426
TITLE: Inhibition of hepatocyte proteolysis and lactate gluconeogenesis by chloroquine
AUTHOR(S): Crabb, David W.; Jersild, Ralph A., Jr.; McCune, Sylvia A.; Swartzentruber, Melanie S.; Harris, Robert A.
CORPORATE SOURCE: Sch. Med., Indiana Univ., Indianapolis, IN, 46223, USA
SOURCE: Archives of Biochemistry and Biophysics (1980), 203(1), 49-57
CODEN: ABBIA4; ISSN: 0003-9861
DOCUMENT TYPE: Journal
LANGUAGE: English

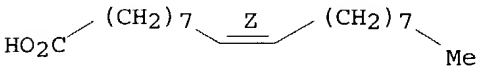
AB Chloroquine (I) [**54-05-7**] (50 μM) is rapidly taken up by isolated hepatocytes in a temperature-dependent manner. I **inhibits** glucose [50-99-7] **synthesis** from lactate [50-21-5], but not from pyruvate [127-17-3] or dihydroxyacetone [96-26-4]. The **inhibition** is reversed by lysine [56-87-1] or ammonia, but not by oleate [**112-80-1**] or carnitine [541-15-1]. Ammonia **inhibits** I uptake by the hepatocytes but lysine does not. I also **inhibits** urea **synthesis**, the release of ninhydrin-reacting substances, the accumulation of amino acids, and the lactate-dependent accumulation of glutamate. Ethanol oxidation in the presence of lactate is also **inhibited**, and this too is reversed by lysine. I increases the redox state of the cytosolic compartment, as evidenced by lactate-to-pyruvate ratios, of hepatocytes prepared from both 48-h fasted and meal-fed rats. The above findings are consistent with I entering the lysosomes of the hepatocytes and **inhibiting** proteolysis by raising the lysosomal pH. Isolated hepatocytes are deficient in amino acids, and I **inhibition** of proteolysis prevents replenishment of the amino acid pools. Thus, I prevents reconstitution of the malate-aspartate shuttle required for the movement of reducing equivalent into the mitochondrion during lactate gluconeogenesis, ethanol oxidation, and glycolysis. The metabolic competency of freshly isolated hepatocytes, therefore, depends on the replenishment of amino acid pools by lysosomal breakdown of endogenous protein. Furthermore, I uptake may be an index of lysosomal function with isolated hepatocytes.

ED Entered STN: 12 May 1984

IT **112-80-1**, biological studies
RL: BIOL (Biological study)
(chloroquine inhibition of hepatocyte lactate gluconeogenesis and proteolysis response to)

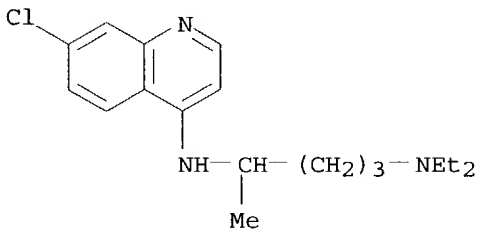
RN 112-80-1 HCAPLUS
CN 9-Octadecenoic acid (9Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



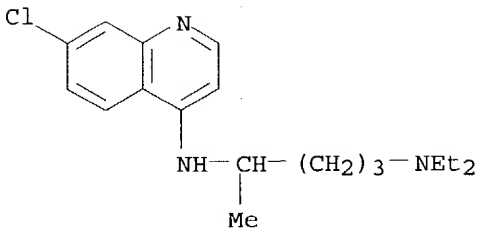
IT **54-05-7**
RL: PRP (Properties)
(hepatocyte lactate gluconeogenesis and proteolysis inhibition by)

RN 54-05-7 HCAPLUS
CN 1,4-Pentanediamine, N4-(7-chloro-4-quinolinyl)-N1,N1-diethyl- (9CI) (CA INDEX NAME)



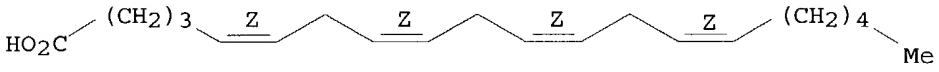
CC 3-5 (Biochemical Interactions)
IT **112-80-1**, biological studies
RL: BIOL (Biological study)
(chloroquine inhibition of hepatocyte lactate gluconeogenesis and proteolysis response to)
IT **54-05-7**
RL: PRP (Properties)
(hepatocyte lactate gluconeogenesis and proteolysis inhibition by)

L181 ANSWER 23 OF 71 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1978:471044 HCAPLUS
DOCUMENT NUMBER: 89:71044
TITLE: Inhibition of hypotensive activity of arachidonic acid in the rat
AUTHOR(S): Damas, J.; Mousty, Jean Claude
CORPORATE SOURCE: Inst. Leon-Fredericq, Univ. Liege, Liege, Belg.
SOURCE: Journal de Pharmacologie (**1978**), 9(1), 13-23
CODEN: JNPHAG; ISSN: 0021-793X
DOCUMENT TYPE: Journal
LANGUAGE: French
AB The influence of various drugs, including several antiinflammatory agents, on hypotensive activity of arachidonic acid [**506-32-1**] was investigated in rats. Aspirin [50-78-2], paracetamol [103-90-2], phenylbutazone [50-33-9], diclofenac [15307-86-5], alclofenac [22131-79-9], ketoprofen [22071-15-4], indomethacin [53-86-1], glafenine [3820-67-5] suppressed this activity. On the other hand, the hypotension was unaffected by sodium salicylate [54-21-7], persantine [58-32-2], escin [6805-41-0], chloroquine [**54-05-7**], dexamethasone [50-02-2], hydrocortisone [50-23-7], di-sodium cromoglycate [15826-37-6], tilidine [20380-58-9], atropine sulfate [55-48-1], methysergide [361-37-5], and promethazine [60-87-7]. The potency of these compds. in **inhibiting** the **synthesis** of prostaglandin in vitro paralleled their ability to affect the hypotensive activity of arachidonic acid in vivo. Thus, measurement of arachidonic acid-induced hypotension in vivo may be useful in accessing the activity of various drugs on prostaglandin formation in vivo and may throw some light on the mech. of action of antiinflammatory agents.
ED Entered STN: 12 May 1984
IT **54-05-7**
RL: BIOL (Biological study)
(hypotension from arachidonic acid response to)
RN 54-05-7 HCAPLUS
CN 1,4-Pentanediamine, N4-(7-chloro-4-quinolinyl)-N1,N1-diethyl- (9CI) (CA INDEX NAME)



IT **506-32-1**
RL: BIOL (Biological study)
(hypotension from, drugs effect on)
RN 506-32-1 HCAPLUS
CN 5,8,11,14-Eicosatetraenoic acid, (5Z,8Z,11Z,14Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

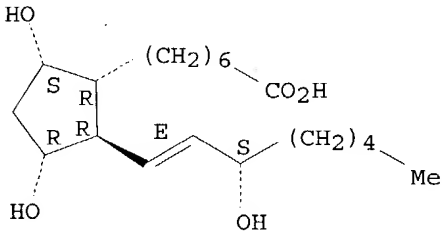


CC 1-5 (Pharmacodynamics)
Section cross-reference(s): 2
IT 50-02-2 50-23-7 50-33-9, biological studies 50-78-2 53-86-1
54-05-7 54-21-7 55-48-1 58-32-2 60-87-7 103-90-2
361-37-5 3820-67-5 6805-41-0 15307-86-5 15826-37-6 22071-15-4
22131-79-9 51931-66-9
RL: BIOL (Biological study)
(hypotension from arachidonic acid response to)
IT **506-32-1**
RL: BIOL (Biological study)
(hypotension from, drugs effect on)

L181 ANSWER 24 OF 71 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1977:25894 HCAPLUS
DOCUMENT NUMBER: 86:25894
TITLE: The effect of anti-inflammatory agents on human synovial fibroblast prostaglandin synthetase
AUTHOR(S): Newcombe, David S.; Ishikawa, Yoshinori
CORPORATE SOURCE: Coll. Med., Univ. Vermont, Burlington, VT, USA
SOURCE: Prostaglandins (1976), 12(5), 849-69
CODEN: PRGLBA; ISSN: 0090-6980
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Human synovial fibroblast prostaglandin **synthetase** [9055-65-6] was **inhibited** by many different nonsteroidal antiinflammatory agents. Aspirin [50-78-2], indomethacin [53-86-1], and phenylbutazone [50-33-9] **inhibited** PGE1 [745-65-3], PGE2 [363-24-6], PGF1α [**745-62-0**], and PGF2α [551-11-1] **synthesis**; whereas D-penicillamine-HCl [2219-30-9] and aurothioglucose [12192-57-3] were more potent **inhibitors** of the F prostaglandins. Histidine [71-00-1] and antimalarials did not **inhibit** human synovial prostaglandin **synthetase.** Hydrocortisone [50-23-7] had no direct effect on prostaglandin **synthetase.** Thus, the proposed **inhibitory** effect of hydrocortisone on prostaglandin production by synovium may be the result of an alteration of enzyme substrate or cofactor concentration rather than a direct

effect on prostaglandin **synthetase.**
ED Entered STN: 12 May 1984
IT **745-62-0**
RL: BIOL (Biological study)
(of synovial fibroblast, inflammation inhibitors effect on)
RN 745-62-0 HCAPLUS
CN Prost-13-en-1-oic acid, 9,11,15-trihydroxy-, (9α,11α,13E,15S)-
(9CI) (CA INDEX NAME)

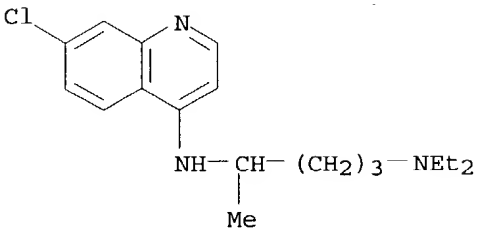
Absolute stereochemistry.
Double bond geometry as shown.



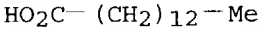
CC 1-4 (Pharmacodynamics)
Section cross-reference(s): 2
IT **Antimalarials**
Inflammation inhibitors
(prostaglandin synthetase of synovial fibroblast response to)
IT 363-24-6 551-11-1 **745-62-0** 745-65-3 9055-65-6
RL: BIOL (Biological study)
(of synovial fibroblast, inflammation inhibitors effect on)

L181 ANSWER 25 OF 71 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1978:145988 HCAPLUS
DOCUMENT NUMBER: 88:145988
TITLE: Relationship between binding of antiinflammatory drugs to albumin and their inhibitory action on prostaglandin synthetase
AUTHOR(S): Robak, Jadwiga; Dembinska-Kiec, Aldona; Panczenko, Bogumila; Gryglewski, Ryszard
CORPORATE SOURCE: Dep. Pharmacol., Med. Acad. Krakow, Krakow, Pol.
SOURCE: Congr. Hung. Pharmacol. Soc., [Proc.] (**1976**), Volume Date 1974, 2(2, Symp. Prostaglandins), 207-10
CODEN: CPSPDT
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Binding of antiinflammatory drugs to hydrophobic sites of albumin is a necessary but not sufficient requirement for inhibition of prostaglandin synthetase [9055-65-6] by these drugs. However, inhibitors of prostaglandin synthetase which are weakly bound to albumin have a better chance to be potent antiinflammatory drugs in vivo than enzymic inhibitors which are strongly bound.
ED Entered STN: 12 May 1984
IT **54-05-7 544-63-8**, biological studies
RL: BIOL (Biological study)
(binding of, by blood serum albumin, prostaglandin **synthetase inhibition** in relation to)
RN 54-05-7 HCAPLUS
CN 1,4-Pentanediamine, N4-(7-chloro-4-quinolinyl)-N1,N1-diethyl- (9CI) (CA

INDEX NAME)



RN 544-63-8 HCAPLUS
CN Tetradecanoic acid (9CI) (CA INDEX NAME)



CC 1-4 (Pharmacodynamics)
IT 50-33-9, biological studies 50-78-2 53-86-1 **54-05-7**
58-15-1 61-68-7 68-89-3 103-90-2 **544-63-8**, biological
studies 642-72-8 644-62-2 3615-24-5 4394-00-7 10166-39-9
13278-36-9 13278-38-1 16524-22-4 22204-53-1 29679-58-1
RL: BIOL (Biological study)
(binding of, by blood serum albumin, prostaglandin **synthetase**
inhibition in relation to)

=> d ibib abs ed hitind 26
YOU HAVE REQUESTED DATA FROM FILE 'WPIX, HCAPLUS, MEDLINE, EMBASE, BIOSIS, BIOTECHDS, BIOTECHNO, DRUGU' - CONTINUE? (Y)/N:y

L181 ANSWER 26 OF 71 MEDLINE on STN DUPLICATE 12
ACCESSION NUMBER: 2001286713 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11255505
TITLE: **Triclosan** and fatty acid synthesis in Plasmodium falciparum: new weapon for an old enemy.
AUTHOR: Bhat G P; Surolia N
CORPORATE SOURCE: Molecular Biology and Genetics Unit, Jawaharlal Nehru Centre for Advanced Scientific Research, Jakkur, Bangalore 560 064, India.
SOURCE: Journal of biosciences, **(2001 Mar)** 26 (1) 1-3.
Journal code: 8100809. ISSN: 0250-5991.
PUB. COUNTRY: India
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 20010529
Last Updated on STN: 20010529
Entered Medline: 20010524
ED Entered STN: 20010529
Last Updated on STN: 20010529
Entered Medline: 20010524
CT Animals
***Antimalarials: PD, pharmacology**

*Fatty Acids: BI, biosynthesis
*Plasmodium falciparum: DE, drug effects
Plasmodium falciparum: ME, metabolism
***Triclosan: PD, pharmacology**
RN **3380-34-5 (Triclosan)**
CN 0 (Antimalarials); 0 (Fatty Acids)

=> d ibib abs ed hitind 27-56
YOU HAVE REQUESTED DATA FROM FILE 'WPIX, HCAPLUS, MEDLINE, EMBASE, BIOSIS, BIOTECHDS, BIOTECHNO, DRUGU' - CONTINUE? (Y)/N:y

L181 ANSWER 27 OF 71 MEDLINE on STN DUPLICATE 14
ACCESSION NUMBER: 95354800 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7628573
TITLE: **Antimalarial** effects of C18 fatty acids on Plasmodium falciparum in culture and on Plasmodium vinckei petteri and Plasmodium yoelii nigeriensis in vivo.
AUTHOR: Krugliak M; Deharo E; Shalmiev G; Sauvain M; Moretti C; Ginsburg H
CORPORATE SOURCE: Department of Biological Chemistry, Hebrew University, Jerusalem, Israel.
SOURCE: Experimental parasitology, **(1995 Aug)** 81 (1) 97-105.
Journal code: 0370713. ISSN: 0014-4894.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199509
ENTRY DATE: Entered STN: 19950921
Last Updated on STN: 19980206
Entered Medline: 19950905

AB Following the demonstration of the **antimalarial** effect of the long chain saturated alcohol n-hentriacontanol ((CH2)29CH2OH), isolated from the Bolivian endemic solanaceous plant Cuatresia sp., we have tested the effect of the C18 **fatty acids** oleic, elaidic, linoleic, and linoleic on **malaria** parasites. These **fatty acids inhibited** the parasitemic development in mice infected with Plasmodium vinckei petteri or with Plasmodium yoelii nigeriensis in a 4-day suppressive test. To gain a deeper discernment of the **antimalarial** mode of action, the effects of these compounds were evaluated on Plasmodium falciparum growth in culture. Whereas n-hentriacontanol did not show any **inhibition** of this parasite, on the contrary, the C18 acids displayed a considerably **inhibitory** activity at < or = 200 micrograms/ml both in intact infected cells and in free parasites. In order to understand the mechanism of their **antimalarial** action, several tests were performed. No hemolysis of infected cells could be observed up to 500 microgram/ml. No effect on the lipid peroxidation, ATP levels, transport through the parasite-induced permeability pathways, or on the phagocytosis of the infected cells could be observed. The cytotoxic effect of the **fatty acids** was very rapid: full **inhibition** of nucleic acids and protein **syntheses** was observed in less than 30 min. This **inhibition** was not relieved by the addition of deferrioxamine or FeCl3, indicating that **fatty acids** (FA) do not act by facilitating the transport of iron. **Inhibition** was relieved in neither the presence of orotic acid or its methyl ester,

indicating that FA do not act at the mitochondrial level of pyrimidine **synthesis.** (ABSTRACT TRUNCATED AT 250 WORDS)
ED Entered STN: 19950921
Last Updated on STN: 19980206
Entered Medline: 19950905
CT Check Tags: Comparative Study; Male
Animals
***Antimalarials: PD, pharmacology**
***Antimalarials: TU, therapeutic use**
*Fatty Acids, Nonesterified: PD, pharmacology
*Fatty Acids, Nonesterified: TU, therapeutic use
Linoleic Acid
Linoleic Acids: PD, pharmacology
Linoleic Acids: TU, therapeutic use
***Malaria: DT, drug therapy**
Mice
Oleic Acid
Oleic Acids: PD, pharmacology
Oleic Acids: TU, therapeutic use
Parasitemia: PC, prevention & control
*Plasmodium: DE, drug effects
*Plasmodium falciparum: DE, drug effects
*Plasmodium yoelii: DE, drug effects
Structure-Activity Relationship
alpha-Linolenic Acid: PD, pharmacology
alpha-Linolenic Acid: TU, therapeutic use
RN 112-79-8 (elaidic acid); 112-80-1 (Oleic Acid); 2197-37-7 (Linoleic Acid); 463-40-1 (alpha-Linolenic Acid)
CN 0 (**Antimalarials**); 0 (Fatty Acids, Nonesterified); 0 (Linoleic Acids); 0 (Oleic Acids)

L181 ANSWER 28 OF 71 MEDLINE on STN DUPLICATE 15
ACCESSION NUMBER: 88293532 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3401244
TITLE: Differential effects of chloroquine on the phospholipid metabolism of Plasmodium-infected erythrocytes.
AUTHOR: Vial H J; Ancelin M L; Thuet M J; Philippot J R
CORPORATE SOURCE: CNRS UA 530, INSERM U 58, Montpellier, France.
SOURCE: Biochemical pharmacology, **(1988 Aug 15)** 37 (16) 3139-47.
Journal code: 0101032. ISSN: 0006-2952.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198809
ENTRY DATE: Entered STN: 19900308
Last Updated on STN: 19970203
Entered Medline: 19880902
AB The effect of the **antimalarial** drug chloroquine (CQ) on the phospholipid metabolism in Plasmodium knowlesi-infected simian erythrocytes has been studied by incubating cells with different labeled precursors and various concentrations of CQ. The drug induced considerable modifications of this metabolism but at the same time decreased nucleic acid and protein **synthesis** as well as the output of 14CO2 from radioactive glucose. Phosphatidylcholine **biosynthesis** was severely reduced. However, under these conditions, CQ had the early effect of markedly increasing phosphatidylinositol labeling from radioactive inositol, **fatty acids**, 1-(14C)palmitoyl-lysophosphatidylcholine, but not from

glycerol. **Synthesis** of phosphatidylserine from (14C)serine and of phosphatidylethanolamine from labeled glycerol, ethanolamine, and serine was increased, especially at high CQ concentrations when the whole metabolism of the parasite was severely reduced. These effects reflect a deep differential effect of CQ on the intense phospholipid metabolism of the Plasmodium-infected erythrocytes, which might involve a redirecting of phospholipid metabolism similar to that induced by other cationic amphiphilic drugs, and a compensatory **synthesis** resulting from the severe **blockage** of phosphatidylcholine **synthesis.**

ED Entered STN: 19900308
Last Updated on STN: 19970203
Entered Medline: 19880902

CT Check Tags: Support, Non-U.S. Gov't
Animals
***Chloroquine: PD, pharmacology**
Erythrocytes: DE, drug effects
*Erythrocytes: ME, metabolism
Fatty Acids: ME, metabolism
Hypoxanthine
Hypoxanthines: ME, metabolism
Isoleucine: ME, metabolism
Macaca fascicularis
***Malaria: BL, blood**
*Phospholipids: BL, blood
Plasmodium

RN 54-05-7 (Chloroquine); 68-94-0 (Hypoxanthine); 73-32-5 (Isoleucine)
CN 0 (Fatty Acids); 0 (Hypoxanthines); 0 (Phospholipids)

L181 ANSWER 29 OF 71 MEDLINE on STN
ACCESSION NUMBER: 2001212630 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11175835
TITLE: New agents to combat malaria.
COMMENT: Comment on: Nat Med. 2001 Feb;7(2):167-73. PubMed ID: 11175846
AUTHOR: Beeson J G; Winstanley P A; McFadden G I; Brown G V
SOURCE: Nature medicine, **(2001 Feb)** 7 (2) 149-50.
Journal code: 9502015. ISSN: 1078-8956.
PUB. COUNTRY: United States
DOCUMENT TYPE: Commentary
News Announcement
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200104
ENTRY DATE: Entered STN: 20010425
Last Updated on STN: 20010425
Entered Medline: 20010419

ED Entered STN: 20010425
Last Updated on STN: 20010425
Entered Medline: 20010419

CT Check Tags: Human
Animals
***Antimalarials: PD, pharmacology**
Drug Resistance
*Oxidoreductases: AI, antagonists & inhibitors
*Plasmodium falciparum: DE, drug effects
***Triclosan: PD, pharmacology**

RN **3380-34-5 (Triclosan)**
CN 0 (Antimalarials); EC 1. (Oxidoreductases); EC 1.3.1.9 (enoyl-(acyl-carrier-protein) reductase (NADH))

L181 ANSWER 30 OF 71 MEDLINE on STN
ACCESSION NUMBER: 97387835 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9243820
TITLE: Effects of secretion inhibitors on the production of CAMP factor from Streptococcus agalactiae.
AUTHOR: Takaisi-Kikuni N B
CORPORATE SOURCE: Laboratoire de Microbiologie Experimentale et Pharmaceutique, Faculte de Pharmacie de l'Universite de Kinshasa, Kinshasa XI, Republique Democratique du Congo.
SOURCE: Cytobios, (1996) 88 (352) 23-33.
Journal code: 0207227. ISSN: 0011-4529.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199709
ENTRY DATE: Entered STN: 19970922
Last Updated on STN: 19970922
Entered Medline: 19970909

AB Investigations of exopeptide secretion with inhibitors were performed to study the synthesis and release of CAMP factor in drug-treated growing cells of Streptococcus agalactiae. Besides a reduction in cell growth, membrane-active substances including **cerulenin** and neuroactive drugs, such as procaine, dibucaine and atropine, increased the CAMP factor activity in culture supernatant. Quinacrine and phenylmethylsulphonyl fluoride, inhibitors of exopeptide-releasing proteases, reduced the bacterial growth, but did not affect the differential rate of the CAMP factor release. Polyanethole sulphonic acid, an anticoagulant preventing cell wall autolysis, promoted cell growth, but caused approximately 40% reduction in the production of CAMP factor from growing cells of S. agalactiae.

ED Entered STN: 19970922
Last Updated on STN: 19970922
Entered Medline: 19970909

CT Check Tags: Comparative Study
Anesthetics, Local: PD, pharmacology
Atropine: PD, pharmacology
*Bacterial Proteins: SE, secretion
Cerulenin: PD, pharmacology
Enzyme Inhibitors: PD, pharmacology
Nalidixic Acid: PD, pharmacology
Polymers: PD, pharmacology
Quinacrine: PD, pharmacology
*Streptococcus agalactiae: DE, drug effects
Streptococcus agalactiae: ME, metabolism
Sulfonic Acids: PD, pharmacology
Tosyl Compounds: PD, pharmacology

RN **17397-89-6 (Cerulenin)**; 389-08-2 (Nalidixic Acid); 455-16-3 (4-toluenesulfonyl fluoride); 51-55-8 (Atropine); 63589-56-0 (poly(anetholesulfonic acid)); 83-89-6 (Quinacrine)

CN 0 (Anesthetics, Local); 0 (Bacterial Proteins); 0 (CAMP protein, Streptococcus); 0 (Enzyme Inhibitors); 0 (Polymers); 0 (Sulfonic Acids); 0 (Tosyl Compounds)

L181 ANSWER 31 OF 71 MEDLINE on STN
ACCESSION NUMBER: 94247631 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7514768
TITLE: ATP regulates synaptic transmission by pre- and postsynaptic mechanisms in guinea-pig myenteric neurons.
AUTHOR: Kamiji T; Morita K; Katayama Y

CORPORATE SOURCE: Department of Autonomic Physiology, Tokyo Medical and Dental University, Japan.
SOURCE: Neuroscience, (**1994 Mar**) 59 (1) 165-74.
Journal code: 7605074. ISSN: 0306-4522.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199406
ENTRY DATE: Entered STN: 19940629
Last Updated on STN: 19960129
Entered Medline: 19940623

AB Intracellular recordings were made from myenteric neurons of the guinea-pig ileum in vitro; they were classified into S and AH neurons according to electrophysiological criteria. ATP (10 **nM-100** microM) inhibited excitatory synaptic potentials in the myenteric plexus; fast excitatory postsynaptic potentials and slow excitatory postsynaptic potentials of S neurons and slow excitatory postsynaptic potentials in AH neurons. This inhibitory action was reversible and dose-dependent, and was usually followed by a transient augmentation of the synaptic potentials after washing of ATP. The actions of ATP on the synaptic potentials were prevented by pretreatment with theophylline, caffeine, quinidine and 8-phenyl theophylline. The ATP analogues, ATP-gamma-s (100 **nM-100** microM) and alpha-beta-methylene ATP (100 **nM-100** microM) also depressed the synaptic potentials recorded from both types of neurons. The inhibitory effect of adenosine on the synaptic potentials was 10 times weaker than that of ATP. Thus, it seems clear that the presynaptic inhibition is not occurring through adenosine A1 or A2 receptors. Furthermore, ATP at high concentrations (> or = 1 microM) augmented nicotinic fast depolarizations of S neurons produced by extracellular acetylcholine. However, ATP at the same concentrations inhibited the slow depolarizations of S and AH neurons caused by exogenous acetylcholine (muscarinic) and substance P. It is concluded that ATP regulates synaptic transmission in the myenteric plexus of the guinea-pig ileum and the sites of ATP actions are pre- and postsynaptic.

ED Entered STN: 19940629
Last Updated on STN: 19960129
Entered Medline: 19940623
CT Check Tags: Support, Non-U.S. Gov't
Adenosine: AA, analogs & derivatives
Adenosine Triphosphate: AA, analogs & derivatives
Adenosine Triphosphate: PD, pharmacology
*Adenosine Triphosphate: PH, physiology
Animals
Bucladesine: PD, pharmacology
Guinea Pigs
*Myenteric Plexus: PH, physiology
*Presynaptic Terminals: PH, physiology
Quinidine: PD, pharmacology
Receptors, Cholinergic: DE, drug effects
Substance P: PD, pharmacology
*Synapses: PH, physiology
Synaptic Transmission: DE, drug effects
*Synaptic Transmission: PH, physiology
Xanthines: PD, pharmacology
RN 33507-63-0 (Substance P); 362-74-3 (Bucladesine); 56-54-2 (Quinidine); 56-65-5 (Adenosine Triphosphate); 58-61-7 (Adenosine)
CN 0 (Receptors, Cholinergic); 0 (Xanthines)

L181 ANSWER 32 OF 71 MEDLINE on STN
ACCESSION NUMBER: 91099410 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2269328
TITLE: Processing without proteolytic cleavage is required for recognition of insulin by T cells.
AUTHOR: Gradehandt G; Hampl J; Milbradt S; Rude E
CORPORATE SOURCE: Institut fur Immunologie, Johannes Gutenberg Universitat, Mainz, FRG.
SOURCE: European journal of immunology, **(1990 Dec)** 20 (12) 2637-41.
Journal code: 1273201. ISSN: 0014-2980.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199102
ENTRY DATE: Entered STN: 19910329
Last Updated on STN: 20000303
Entered Medline: 19910220

AB Beef insulin as well as a chymotryptic A-chain fragment [BI-A1-14(SSO3-)3] need uptake by antigen-presenting cells (APC) for efficient presentation in combination with major histocompatibility complex class II molecules to insulin-specific T cells. This could be shown by the inability of aldehyde-fixed APC to present these antigens to T cells. Furthermore, presentation of the insulin fragment as well as presentation of ovalbumin (OVA) was inhibited by treatment of APC with chloroquine, **cerulenin** or tunicamycin. This was not the case for a processing-independent OVA peptide. Treatment of APC during antigen pulsing with various protease inhibitors, active on all classes of proteases, did not block presentation of insulin although some of these reagents did interfere with the presentation of OVA. Several inhibitors especially of serine or thiol proteases rather enhanced the presentation of insulin. This indicates that intracellular proteolytic cleavage of insulin does not seem to be required for generation of the antigenic determinant but, if it occurs, rather destroys the antigenic peptide. Insulin and its A-chain fragment may, therefore, represent a model for a processing-dependent antigen not requiring proteolytic cleavage but other modifications.

ED Entered STN: 19910329
Last Updated on STN: 20000303
Entered Medline: 19910220

CT Check Tags: In Vitro; Support, Non-U.S. Gov't
Animals
Antigen-Presenting Cells: IM, immunology
Antigen-Presenting Cells: ME, metabolism
Cell Line
Chloroquine: PD, pharmacology
Endocytosis
Endopeptidases: ME, metabolism
*Insulin: IM, immunology
Insulin: ME, metabolism
Mice
Ovalbumin: IM, immunology
Ovalbumin: ME, metabolism
Protease Inhibitors: PD, pharmacology
*T-Lymphocytes: IM, immunology
Tunicamycin: PD, pharmacology

RN 11061-68-0 (Insulin); 11089-65-9 (Tunicamycin); 54-05-7 (Chloroquine); 9006-59-1 (Ovalbumin)

CN 0 (Protease Inhibitors); EC 3.4.- (Endopeptidases)

L181 ANSWER 33 OF 71 MEDLINE on STN
ACCESSION NUMBER: 89382362 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2476557
TITLE: Adenosine 5'-triphosphate modulates membrane potassium conductance in guinea-pig myenteric neurones.
AUTHOR: Katayama Y; Morita K
CORPORATE SOURCE: Department of Autonomic Physiology, Tokyo Medical and Dental University, Japan.
SOURCE: Journal of physiology, (**1989 Jan**) 408 373-90.
Journal code: 0266262. ISSN: 0022-3751.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198910
ENTRY DATE: Entered STN: 19900309
Last Updated on STN: 19960129
Entered Medline: 19891025

AB 1. Intracellular recordings were made from myenteric neurones isolated from the guinea-pig small intestine to study actions of adenosine 5'-triphosphate (ATP). ATP was applied by superfusion (10 **nM-100** microM) or pressure ejection from ATP-containing glass pipettes. 2. Myenteric neurones have been classified into two groups: type I/S neurones and type II/AH neurones. ATP produced a membrane hyperpolarization in 80% of AH neurones and a membrane depolarization in 90% of S neurones in a dose-dependent manner. Adenosine caused responses similar to those induced by ATP in both AH and S neurones, but was less effective than ATP. 3. The ATP-induced hyperpolarization was associated with a fall in input resistance, but the ATP-induced depolarization was accompanied by an increase in input resistance. Both responses reversed in polarity near the potassium equilibrium potential (-84 to -87 mV) and the reversal potential varied with extracellular potassium concentration, as predicted by the Nernst equation. These results indicate that the hyperpolarization is due to an increase, while the depolarization is due to a decrease in potassium conductance. 4. Both the hyperpolarization and the depolarization induced by ATP persisted in calcium-free solution containing 1.2 mM-magnesium, but were markedly reduced or abolished in calcium-free solutions containing 3.7-10 mM-magnesium and by 1 mM-nickel or cobalt. Both responses to ATP persisted in tetraethylammonium (1-10 mM) or tetrodotoxin (1-3 microM)-containing solutions. 5. Quinine and quinidine (1-100 microM) reversibly depressed both the ATP-induced responses. Caffeine (100 microM), theophylline (100 microM) and 3-isobutyl-1-methylxanthine (1-10 microM) did not significantly affect the ATP-induced depolarization but did reversibly depress the ATP-induced hyperpolarization. 6. These results suggest that the ATP-induced hyperpolarization may be due to activation, and the ATP-induced depolarization to inactivation, of a calcium-sensitive potassium conductance.

ED Entered STN: 19900309
Last Updated on STN: 19960129
Entered Medline: 19891025

CT Check Tags: Support, Non-U.S. Gov't
Action Potentials: DE, drug effects
Adenosine: PD, pharmacology
*Adenosine Triphosphate: PD, pharmacology
Animals
Guinea Pigs
*Intestine, Small: IR, innervation
Membrane Potentials: DE, drug effects

*Neurons: PH, physiology
Potassium: PD, pharmacology
Quinidine: PD, pharmacology
Quinine: PD, pharmacology
Substance P: PD, pharmacology
Tetraethylammonium Compounds: PD, pharmacology
Tetrodotoxin: PD, pharmacology
RN 130-95-0 (Quinine); 33507-63-0 (Substance P); 4368-28-9 (Tetrodotoxin); 56-54-2 (Quinidine); 56-65-5 (Adenosine Triphosphate); 58-61-7 (Adenosine); 7440-09-7 (Potassium)
CN 0 (Tetraethylammonium Compounds)

L181 ANSWER 34 OF 71 MEDLINE on STN
ACCESSION NUMBER: 89124735 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2783724
TITLE: Requirements for histoplasmin presentation by accessory cells to a Histoplasma capsulatum-reactive T-cell line.
AUTHOR: Harris J E; Deepe G S Jr
CORPORATE SOURCE: Department of Medicine, University of Cincinnati College of Medicine, OH 45267.
CONTRACT NUMBER: AI 23017 (NIAID)
K04 AI 00856 (NIAID)
SOURCE: Journal of leukocyte biology, **(1989 Feb)** 45 (2) 105-13.
Journal code: 8405628. ISSN: 0741-5400.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198903
ENTRY DATE: Entered STN: 19900308
Last Updated on STN: 19980206
Entered Medline: 19890321

AB We examined the pathways involved in presentation of native histoplasmin by adherent splenocytes (as a source of accessory cells) to JC1, a Histoplasma capsulatum-reactive murine T-cell line that is CD4+. JC1 did not respond to accessory cells that had been fixed with paraformaldehyde and then exposed to histoplasmin but did proliferate to antigen-pulsed cells that were subsequently fixed. Accessory cells that were coincubated with histoplasmin and sodium azide or 2-deoxy-D-glucose failed to induce proliferation of JC1. Moreover, accessory cells exposed to the lysosomotropic agents, chloroquine and ammonium chloride, were unable to present antigen. Monensin also inhibited presentation of histoplasmin if added to accessory cells concomitant with antigen. In contrast, accessory cells that had been pulsed with antigen for 2 hr and then exposed to each inhibitor for 2 hr stimulated proliferation of JC1. The antigen-presenting capacity of accessory cells that had been pulsed with histoplasmin for 2 hr was diminished considerably by subsequent treatment with phospholipase A2. Additional studies demonstrated that **cerulenin**, which depresses posttranslational lipid modification of proteins, abolished presentation of histoplasmin. The reactivity of JC1 was sharply reduced by anti-L3T4 (CD4) or by anti-I-Ab monoclonal antibody. The results not only indicate that presentation of histoplasmin requires active metabolic events within accessory cells, they also delineate the pathways involved in handling this antigen.

ED Entered STN: 19900308
Last Updated on STN: 19980206
Entered Medline: 19890321
CT Check Tags: Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Ammonium Chloride

Animals
Antibodies, Monoclonal: PH, physiology
Antigen-Presenting Cells: DE, drug effects
*Antigen-Presenting Cells: IM, immunology
*Antigens, Fungal: IM, immunology
Azides: PD, pharmacology
Cell Line
Cerulenin: PD, pharmacology
Chloroquine
Deoxyglucose: PD, pharmacology
Formaldehyde
*Histoplasma: IM, immunology
*Histoplasmin: IM, immunology
Immunosuppressive Agents: PD, pharmacology
Mice
Mice, Inbred C57BL
Monensin: PD, pharmacology
Phospholipases A
Polymers
Protease Inhibitors
Sodium Azide
*T-Lymphocytes: IM, immunology
Temperature

RN 12125-02-9 (Ammonium Chloride); 154-17-6 (Deoxyglucose); 17090-79-8 (Monensin); **17397-89-6 (Cerulenin)**; 26628-22-8 (Sodium Azide); 30525-89-4 (paraform); 50-00-0 (Formaldehyde); 54-05-7 (Chloroquine); 9008-05-3 (Histoplasmin)

CN 0 (Antibodies, Monoclonal); 0 (Antigens, Fungal); 0 (Azides); 0 (Immunosuppressive Agents); 0 (Polymers); 0 (Protease Inhibitors); EC 3.1.1.- (Phospholipases A)

L181 ANSWER 35 OF 71 MEDLINE on STN
ACCESSION NUMBER: 88078055 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3334857
TITLE: Acyl-CoA synthetase activity in Plasmodium knowlesi-infected erythrocytes displays peculiar substrate specificities.
AUTHOR: Beaumelle B D; Vial H J
CORPORATE SOURCE: UA 530 CNRS, INSERM U.58, Montpellier, France.
SOURCE: Biochimica et biophysica acta, **(1988 Jan 19)** 958 (1) 1-9.
Journal code: 0217513. ISSN: 0006-3002.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198802
ENTRY DATE: Entered STN: 19900305
Last Updated on STN: 19980206
Entered Medline: 19880225

AB In its blood stages the **malaria** parasite, Plasmodium, displays very high lipid metabolism. We present evidence for an abundant long-chain acyl-CoA **synthetase** (EC 6.2.1.3) activity in Plasmodium knowlesi-infected simian erythrocytes. The activity was found to be 20-fold higher in the schizont-infected (the last parasite stage) than in control erythrocytes. The cosubstrate requirements of the enzyme were similar to those previously reported for acyl-CoA **synthetases** from other sources. Among the separated reaction products of oleyl-CoA **synthetase**, only PPi and oleyl-CoA were **inhibitory**, with Ki over 350 microM. The **fatty acid** specificity of the

parasite acyl-CoA **synthetase** activity was fairly marked and depended on the unsaturation state of the substrate. The tested **fatty acids** displayed similar Vmax, whereas their Km ranged from 11 (palmitate) to 59 microM (arachidonate). Finally, experiments involving heat inactivation and separation on hydroxyapatite excluded the presence of a specific arachidonyl-CoA **synthetase** identical to those present in other cells. On the other hand, **fatty acid** competition experiments evidenced the existence of at least two distinct enzymatic sites for **fatty acid** activation in P. knowlesi-infected simian erythrocytes: one is specific for saturated **fatty acids** and the other for polyunsaturated species, whereas oleate could be activated at both sites.

ED Entered STN: 19900305
Last Updated on STN: 19980206
Entered Medline: 19880225

CT Check Tags: Comparative Study; Support, Non-U.S. Gov't
Animals
*Coenzyme A Ligases: BL, blood
*Erythrocytes: EN, enzymology
Erythrocytes: PS, parasitology
Kinetics
Macaca fascicularis
Macaca mulatta
Malaria: BL, blood
***Malaria: EN, enzymology**
Plasmodium: PY, pathogenicity
Reference Values
Substrate Specificity

CN EC 6.2.1. (Coenzyme A Ligases)

L181 ANSWER 36 OF 71 / MEDLINE on STN
ACCESSION NUMBER: 88088738 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3693897
TITLE: **Cerulenin** is a potent inhibitor of antigen processing by antigen-presenting cells.
AUTHOR: Falo L D Jr; Benacerraf B; Rothstein L; Rock K L
CORPORATE SOURCE: Department of Pathology, Harvard Medical School, Boston, MA 02115.
CONTRACT NUMBER: AI 20248 (NIAID)
CA 14723 (NCI)
R01 14732
SOURCE: Journal of immunology (Baltimore, Md. : 1950), **(1987 Dec 15)** 139 (12) 3918-23.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 198801
ENTRY DATE: Entered STN: 19900305
Last Updated on STN: 19970203
Entered Medline: 19880125

AB **Cerulenin** is an antibiotic that inhibits eukaryotic lipid and sterol synthesis and blocks lipid modification of proteins. The effect of **cerulenin** on the ability of accessory cells to present antigen to T cells was investigated. This antibiotic strongly inhibits the ability of accessory cells to present antigen to murine T-T hybrids. This effect is observed for multiple distinct antigens including L-glutamic acid60-L-alanine30-L-tyrosine10, bovine insulin, L-glutamic

acid56-L-lysine35-L-phenylalanine9, and ovalbumen. Presentation by both macrophage and B lymphoblastoid cell lines is inhibited. The ability to effectively pulse these cells with antigen is inhibited but not the ability of these same cells to present antigen that they have previously processed. Furthermore, this inhibition is selective as it can occur without significant inhibition of the antigen-presenting cell protein or DNA synthesis. **Cerulenin** does not inhibit antigen uptake or catabolism as assessed with labeled antigen. By these criteria this drug is shown to interfere with an antigen-processing step. The ability of **cerulenin** to block processing was compared with other known inhibitors. Although **cerulenin** was effective with all antigens tested, at least one inhibitor was not. Taken together, these results suggest that the effect of **cerulenin** may define a distinct step in antigen processing and provides evidence that some other processing events are not universally required. The ability of **cerulenin** to interfere with antigen processing is discussed in the context of the known actions of this antibiotic and events of antigen processing and presentation.

ED Entered STN: 19900305
Last Updated on STN: 19970203
Entered Medline: 19880125

CT Check Tags: Comparative Study; Support, U.S. Gov't, P.H.S.
Ammonium Chloride: PD, pharmacology
Animals
*Antibiotics, Antifungal: PD, pharmacology
*Antigen-Presenting Cells: DE, drug effects
Antigen-Presenting Cells: IM, immunology
*Antigens: IM, immunology
Cell Line
***Cerulenin: PD, pharmacology**
Chloroquine: PD, pharmacology
Depression, Chemical
Lymphocyte Activation
Mice
Monensin: PD, pharmacology

RN 12125-02-9 (Ammonium Chloride); 17090-79-8 (Monensin); **17397-89-6 (Cerulenin)**; 54-05-7 (Chloroquine)

CN 0 (Antibiotics, Antifungal); 0 (Antigens)

L181 ANSWER 37 OF 71 MEDLINE on STN
ACCESSION NUMBER: 82158935 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7337434
TITLE: Secretion of staphylocoagulase be Staphylococcus aureus: the role of a cell-bound intermediate.
AUTHOR: Engels W; Kamps M A
SOURCE: Antonie van Leeuwenhoek, **(1981)** 47 (6) 509-24.
Journal code: 0372625. ISSN: 0003-6072.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198205
ENTRY DATE: Entered STN: 19900317
Last Updated on STN: 19900317
Entered Medline: 19820521

AB A cell-bound staphylocoagulase could be detected in chemostat cultures of Staphylococcus aureus 104 under magnesium-and oxygen-limited growth conditions. A distribution study revealed that 81% of the enzyme was membrane-bound and could be optimally released by Triton X-100. The remaining part was located in the periplasmic space and was released

during protoplasting of organism. From inhibition studies with **cerulenin**, quinacrine, lincomycin an chloramphenicol, it was concluded that the cell-bound form was precursor in the secretion of extracellular staphylocoagulase. The involvement of a lipid intermediate/exoprotein-releasing protease system in the secretion of staphylocoagulase, and of exoproteins in general, is discussed.

ED Entered STN: 19900317
Last Updated on STN: 19900317
Entered Medline: 19820521

CT Cell Membrane: EN, enzymology
Cerulenin: PD, pharmacology
Chloramphenicol: PD, pharmacology
*Coagulase: ME, metabolism
Lincomycin: PD, pharmacology
Protoplasts: EN, enzymology
Quinacrine: PD, pharmacology
Sodium Chloride: PD, pharmacology
Staphylococcus aureus: DE, drug effects
*Staphylococcus aureus: EN, enzymology

RN 154-21-2 (Lincomycin); **17397-89-6 (Cerulenin)**; 56-75-7 (Chloramphenicol); 7647-14-5 (Sodium Chloride); 83-89-6 (Quinacrine)

CN 0 (Coagulase)

L181 ANSWER 38 OF 71 MEDLINE on STN
ACCESSION NUMBER: 82134198 MEDLINE
DOCUMENT NUMBER: PubMed ID: 6277266
TITLE: Regulation of exoprotease production by temperature and oxygen in Vibrio alginolyticus.
AUTHOR: Hare P; Long S; Robb F T; Woods D R
SOURCE: Archives of microbiology, **(1981 Dec)** 130 (4) 276-80.
Journal code: 0410427. ISSN: 0302-8933.
PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198204
ENTRY DATE: Entered STN: 19900317
Last Updated on STN: 19900317
Entered Medline: 19820412

AB The production of an extracellular collagenase and alkaline protease by Vibrio alginolyticus during stationary phase was inhibited by a temperature shift from 30 to 37 degrees C and by a lack of oxygen. The stability of the exoproteases was unaffected by incubation at 37 degrees C and aeration. The optimum growth temperature for the V. alginolyticus strain was 33.5 degrees C and there was no difference in the growth rate at 30 and 37 degrees C. Aeration enhanced the rate of growth of exponential phase cells. Temperature and oxygen did not affect the growth of stationary phase cells when the exoproteases were being produced. Macromolecular synthesis in stationary phase cells was not affected by temperature. There was no rapid release of the exoproteases after temperature shift down and chloramphenicol inhibited the production of the enzymes when added at time of temperature shift down from 37 to 30 degrees C. The regulation of exoprotease production by temperature and oxygen was specific and has implications regarding the ecology of V. alginolyticus. **Cerulenin**, quinacrine and O-phenanthroline inhibited the production of the exoproteases.

ED Entered STN: 19900317
Last Updated on STN: 19900317
Entered Medline: 19820412

CT **Cerulenin: PD, pharmacology**
Microbial Collagenase: ME, metabolism
Oxygen
*Peptide Hydrolases: ME, metabolism
Peptide Hydrolases: SE, secretion
Quinacrine: PD, pharmacology
Secretory Rate: DE, drug effects
Temperature
*Vibrio: EN, enzymology
RN **17397-89-6 (Cerulenin)**; 7782-44-7 (Oxygen); 83-89-6 (Quinacrine)
CN EC 3.4 (Peptide Hydrolases); EC 3.4.24.3 (Microbial Collagenase)

L181 ANSWER 39 OF 71 MEDLINE on STN
ACCESSION NUMBER: 80136306 MEDLINE
DOCUMENT NUMBER: PubMed ID: 6444621
TITLE: Requirements for fatty acid synthesis and a chelation-sensitive step in the production of glucosyltransferase by Streptococcus mutans.
AUTHOR: Kuramitsu H K; Wondrack L
SOURCE: Infection and immunity, **(1980 Jan)** 27 (1) 107-12.
Journal code: 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198005
ENTRY DATE: Entered STN: 19900315
Last Updated on STN: 19900315
Entered Medline: 19800523
AB The antibiotic **cerulenin** differentially inhibited the production of glucosyltransferase activity by Streptococcus mutans GS5. **Cerulenin** preferentially inhibited [14C]acetate incorporation into cellular lipids but did not affect protein synthesis or ribonucleic acid synthesis in the same manner. No significant intracellular accumulation of glucosyltransferase activity could be demonstrated in cultures treated with **cerulenin.** On the other hand, another inhibitor of lipid synthesis, sodium chlorophenoxyisobutyrate, did not differentially inhibit glucosyltransferase expression. In addition, the role of a metal-requiring protease in the production of glucosyltransferase activity was suggested by the observation that the chelator quinacrine differentially inhibited the production of the enzyme.
ED Entered STN: 19900315
Last Updated on STN: 19900315
Entered Medline: 19800523
CT Check Tags: Support, U.S. Gov't, P.H.S.
Cerulenin: PD, pharmacology
*Chelating Agents: PD, pharmacology
*Fatty Acids: BI, biosynthesis
*Glucosyltransferases: BI, biosynthesis
Glucosyltransferases: ME, metabolism
Protease Inhibitors: ME, metabolism
Quinacrine: PD, pharmacology
Streptococcus mutans: DE, drug effects
*Streptococcus mutans: ME, metabolism
RN **17397-89-6 (Cerulenin)**; 83-89-6 (Quinacrine)
CN 0 (Chelating Agents); 0 (Fatty Acids); 0 (Protease Inhibitors); EC 2.4.1.- (Glucosyltransferases)

L181 ANSWER 40 OF 71 MEDLINE on STN
ACCESSION NUMBER: 79173007 MEDLINE

DOCUMENT NUMBER: PubMed ID: 108256
TITLE: Export of extracellular levansucrase by Bacillus subtilis: inhibition by **cerulenin** and quinacrine.
AUTHOR: Caulfield M P; Berkeley R C; Pepper E A; Melling J
SOURCE: Journal of bacteriology, **(1979 May)** 138 (2) 345-51.
Journal code: 2985120R. ISSN: 0021-9193.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197907
ENTRY DATE: Entered STN: 19900315
Last Updated on STN: 19900315
Entered Medline: 19790728

AB Bacillus subtilis B secretes an inducible, extracellular enzyme, levansucrase. Inhibition studies were undertaken to investigate the possible mechanism of release of this enzyme. The antibiotic **cerulenin**, at a concentration of 10 micrograms/ml, totally inhibited de novo lipid synthesis in B. subtilis B for at least 1 h, while only slightly reducing protein and RNA synthesis. At this concentration **cerulenin**, added concomitantly with the inducer sucrose, prevented the release of levansucrase for at least 150 min. This was not due to the prevention of inducer uptake by the cells. The release of the enzyme was also independent of cell division. In B. subtilis 1007 the induction of beta-galactosidase by 5 mM lactose was not prevented by **cerulenin** . Preliminary evidence indicated the association of a lipid moiety with the enzyme as it passes through the cytoplasmic membrane. Quinacrine (0.2 mM), which inhibits the penicillinase-releasing protease of Bacillus licheniformis, inhibited levansucrase release from B. subtilis B, but had no effect on lipid synthesis.

ED Entered STN: 19900315
Last Updated on STN: 19900315
Entered Medline: 19790728

CT *Antibiotics, Antifungal: PD, pharmacology
*Bacillus subtilis: DE, drug effects
Bacillus subtilis: EN, enzymology
Bacillus subtilis: ME, metabolism
Bacterial Proteins: BI, biosynthesis
***Cerulenin: PD, pharmacology**
Depression, Chemical
Fructans
*Hexosyltransferases: ME, metabolism
Lipids: BI, biosynthesis
***Quinacrine: PD, pharmacology**
RNA, Bacterial: BI, biosynthesis
Sucrose: ME, metabolism
beta-Galactosidase: BI, biosynthesis

RN **17397-89-6 (Cerulenin)**; 57-50-1 (Sucrose); 83-89-6 (Quinacrine)

CN 0 (Antibiotics, Antifungal); 0 (Bacterial Proteins); 0 (Fructans); 0 (Lipids); 0 (RNA, Bacterial); EC 2.4.1.- (Hexosyltransferases); EC 3.2.1.23 (beta-Galactosidase)

L181 ANSWER 41 OF 71 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN DUPLICATE 2

ACCESSION NUMBER: 2002:163693 BIOSIS
DOCUMENT NUMBER: PREV200200163693
TITLE: Genomics, pathogenesis and control of infection with protozoan parasites.
AUTHOR(S): Teixeira, Santuza M. R. [Reprint author]; Vieira, Leda Q.

[Reprint author]; Gazzinelli, Ricardo T. [Reprint author]
CORPORATE SOURCE: Dept of Biochemistry and Immunology, Federal University of Minas Gerais, Av. Antonio carlos 6627, 31270-901, Belo Horizonte, MG, Brazil
santuzat@mono.icb.ufmg.br
SOURCE: Trends in Parasitology, (February, 2002) Vol. 18, No. 2, pp. 52-54. print.
Meeting Info.: The XXVIII Annual Meeting of Basic Research on Chagas Disease and the XVII Annual Meeting of the Brazilian Society of Protozoology. Caxambu, Minas Gerais, Brazil. November 05-07, 2001. Brazilian Society of Protozoology.
ISSN: 1471-4922.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Report; (Meeting Report)
LANGUAGE: English
ENTRY DATE: Entered STN: 5 Mar 2002
Last Updated on STN: 5 Mar 2002
ED Entered STN: 5 Mar 2002
Last Updated on STN: 5 Mar 2002
CC Cytology - General 02502
Cytology - Animal 02506
Cytology - Human 02508
Genetics - General 03502
Genetics - Animal 03506
Genetics - Human 03508
Biochemistry studies - Proteins, peptides and amino acids 10064
Pathology - Therapy 12512
Cardiovascular system - Heart pathology 14506
Endocrine - General 17002
Integumentary system - Pathology 18506
Pharmacology - General 22002
Pharmacology - Clinical pharmacology 22005
Immunology - General and methods 34502
Immunology - Immunopathology, tissue immunology 34508
Immunology, parasitological 35000
Public health: epidemiology - Communicable diseases 37052
Public health: epidemiology - Organic diseases and neoplasms 37054
Public health: epidemiology - Miscellaneous 37056
Public health: disease vectors - General 37057
Chemotherapy - General, methods and metabolism 38502
Chemotherapy - Antiparasitic agents 38510
Parasitology - General 60502
Parasitology - Medical 60504
Invertebrata: comparative, experimental morphology, physiology and pathology - Protozoa 64002
Invertebrata: comparative, experimental morphology, physiology and pathology - Insecta: physiology 64076
IT Major Concepts
Genetics; Immune System (Chemical Coordination and Homeostasis); Parasitology; Pharmacology
IT Diseases
Chagas disease: parasitic disease, etiology
Chagas Disease (MeSH)
IT Diseases
Plasmodium infection: parasitic disease
Malaria (MeSH)
IT Diseases
inflammation: immune system disease
Inflammation (MeSH)

IT Diseases
leishmaniasis: integumentary system disease, parasitic disease, epidemiology
Leishmaniasis (MeSH)
IT Diseases
myocarditis: heart disease
Myocarditis (MeSH)
IT Diseases
protozoan infection: parasitic disease, etiology, prevention and control, therapy
IT Chemicals & Biochemicals
interferon-gamma [IFN-gamma]; triazole derivatives: antiinfective-drug, antiparasitic-drug, antiprotozoal-drug; **triclosan**: antiinfective-drug, antiparasitic-drug, antiprotozoal-drug
IT Methods & Equipment
chemotherapy: therapeutic method; immunotherapy: immunologic method, therapeutic method
IT Miscellaneous Descriptors
cell biology; disease susceptibility; genetic variability; genomics; host resistance; immunology; pathogenesis; vaccine development; vector biology; vector resistance; Meeting Report
ORGN Classifier
Diptera 75314
Super Taxa
Insecta; Arthropoda; Invertebrata; Animalia
Organism Name
Anopheles stephensi: disease vector, mosquito, transgenic
Drosophila melanogaster: animal model, host
Taxa Notes
Animals, Arthropods, Insects, Invertebrates
ORGN Classifier
Flagellata 35200
Super Taxa
Protozoa; Invertebrata; Animalia
Organism Name
Leishmania major: parasite
Trypanosoma brucei: parasite
Trypanosoma cruzi: parasite
Taxa Notes
Animals, Invertebrates, Microorganisms, Protozoans
ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human: host, patient
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates
ORGN Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
mouse: animal model, host
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates
ORGN Classifier
Protozoa 35000
Super Taxa

Invertebrata; Animalia
Organism Name
protozoa: parasite
Taxa Notes
Animals, Invertebrates, Microorganisms, Protozoans
ORGN Classifier
Sporozoa 35400
Super Taxa
Protozoa; Invertebrata; Animalia
Organism Name
Plasmodium: parasite
Plasmodium yoelii
Taxa Notes
Animals, Invertebrates, Microorganisms, Protozoans
RN **3380-34-5 (triclosan)**

L181 ANSWER 42 OF 71 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN DUPLICATE 13
ACCESSION NUMBER: 1998:495881 BIOSIS
DOCUMENT NUMBER: PREV199800495881
TITLE: Nuclear-encoded proteins target to the plastid in Toxoplasma gondii and Plasmodium falciparum.
AUTHOR(S): Waller, Ross F.; Keeling, Patrick J.; Donald, Robert G. K.; Striepen, Boris; Handman, Emanuel; Lang-Unnasch, Naomi; Cowman, Alan F.; Besra, Gurdyal S.; Roos, David S.; McFadden, Geoffrey I. [Reprint author]
CORPORATE SOURCE: Plant Cell Biol. Res. Centre, Sch. Bot., Univ. Melbourne, Parkville, VIC 3052, Australia
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (Oct. 13, 1998) Vol. 95, No. 21, pp. 12352-12357. print.
CODEN: PNASA6. ISSN: 0027-8424.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 18 Nov 1998
Last Updated on STN: 18 Nov 1998

AB A vestigial, **nonphotosynthetic** plastid has been identified recently in protozoan parasites of the phylum Apicomplexa. The apicomplexan plastid, or "apicoplast," is indispensable, but the complete sequence of both the Plasmodium falciparum and Toxoplasma gondii apicoplast genomes has offered no clue as to what essential metabolic function(s) this organelle might perform in parasites. To investigate possible functions of the apicoplast, we sought to identify nuclear-encoded genes whose products are **targeted** to the apicoplast in Plasmodium and Toxoplasma. We describe here nuclear genes encoding ribosomal proteins S9 and L28 and the **fatty acid biosynthetic** enzymes acyl carrier protein (ACP), beta-ketoacyl-ACP **synthase** III (FabH), and beta-hydroxyacyl-ACP dehydratase (FabZ). These genes show high similarity to plastid homologues, and immunolocalization of S9 and ACP verifies that the proteins accumulate in the plastid. All the putatively apicoplast-**targeted** proteins bear N-terminal presequences consistent with plastid **targeting**, and the ACP presequence is shown to be sufficient to **target** a recombinant green fluorescent protein reporter to the apicoplast in transgenic T. gondii. Localization of ACP, and very probably FabH and FabZ, in the apicoplast implicates **fatty acid biosynthesis** as a likely function of the apicoplast. Moreover, **inhibition** of P. falciparum growth by thiolactomycin, an **inhibitor** of FabH, indicates a vital role for apicoplast **fatty acid biosynthesis.**

Because the **fatty acid biosynthesis** genes identified here are of a plastid/bacterial type, and distinct from those of the equivalent pathway in animals, **fatty acid biosynthesis** is potentially an excellent **target** for therapeutics directed against **malaria**, toxoplasmosis, and other apicomplexan-mediated diseases.

ED Entered STN: 18 Nov 1998
Last Updated on STN: 18 Nov 1998
CC Genetics - Animal 03506
Biochemistry studies - Nucleic acids, purines and pyrimidines 10062
Metabolism - Lipids 13006
Parasitology - Medical 60504
Invertebrata: general and systematic - Protozoa 63502
IT Major Concepts
Metabolism; Molecular Genetics (Biochemistry and Molecular Biophysics)
IT Parts, Structures, & Systems of Organisms
apicoplast, metabolic function, nonphotosynthetic plastid
IT Diseases
malaria: blood and lymphatic disease, parasitic disease
Malaria (MeSH)
IT Chemicals & Biochemicals
fatty acid biosynthesis genes; nuclear-encoded proteins
IT Miscellaneous Descriptors
fatty acid biosynthesis; organellar targeting
ORGN Classifier
Sporozoa 35400
Super Taxa
Protozoa; Invertebrata; Animalia
Organism Name
Plasmodium-falciparum: apicomplexan parasite
Toxoplasma-gondii: apicomplexan parasite
Taxa Notes
Animals, Invertebrates, Microorganisms, Protozoans

L181 ANSWER 43 OF 71 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 2000:543330 BIOSIS
DOCUMENT NUMBER: PREV200000543330
TITLE: Pyrithione: An industrial biocide that kills Plasmodium in vitro and in vivo, disrupts PMF, and whose use does not result in resistance.
AUTHOR(S): Geiger, J. R. [Reprint author]; Vinopal, R. T.; Stopka, J. M.
CORPORATE SOURCE: Arch Chemicals, Cheshire, CT, USA
SOURCE: Abstracts of the Interscience Conference on Antimicrobial Agents and Chemotherapy, (2000) Vol. 40, pp. 515. print.
Meeting Info.: 40th Interscience Conference on Antimicrobial Agents and Chemotherapy. Toronto, Ontario, Canada. September 17-20, 2000.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 13 Dec 2000
Last Updated on STN: 11 Jan 2002
ED Entered STN: 13 Dec 2000
Last Updated on STN: 11 Jan 2002
CC Pest control: general, pesticides and herbicides 54600
General biology - Symposia, transactions and proceedings 00520
Pathology - Therapy 12512
Pharmacology - General 22002

Parasitology - General 60502
Invertebrata: comparative, experimental morphology, physiology and pathology - Protozoa 64002
IT Major Concepts
Parasitology; Pharmacology
IT Chemicals & Biochemicals
pyrithione: anti-dandruff agent, biocide, industrial, mode of action; **triclosan**: biocide
IT Miscellaneous Descriptors
Meeting Abstract
ORGN Classifier
Annonaceae 25575
Super Taxa
Dicotyledones; Angiospermae; Spermatophyta; Plantae
Organism Name
Polyalthia nemoralis: **antimalarial** effects, medicinal plant
Taxa Notes
Angiosperms, Dicots, Plants, Spermatophytes, Vascular Plants
ORGN Classifier
Sporozoa 35400
Super Taxa
Protozoa; Invertebrata; Animalia
Organism Name
Plasmodium falciparum: parasite
Taxa Notes
Animals, Invertebrates, Microorganisms, Protozoans
RN 1121-30-8 (pyrithione)
3380-34-5 (triclosan)

L181 ANSWER 44 OF 71 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 2000:112613 BIOSIS
DOCUMENT NUMBER: PREV200000112613
TITLE: Biosynthesis of glycosylphosphatidylinositols of Plasmodium falciparum in a cell-free incubation system: Inositol acylation is needed for mannosylation of glycosylphosphatidylinositols.
AUTHOR(S): Gerold, Peter; Jung, Nicole; Azzouz, Nahid; Freiberg, Nicole; Kobe, Sabine; Schwarz, Ralph T. [Reprint author]
CORPORATE SOURCE: Medizinisches Zentrum fuer Hygiene und Medizinisches Mikrobiologie, Phillipps-Universitaet, Robert-Koch Strasse 17, D-35037, Marburg, Germany
SOURCE: Biochemical Journal, (Dec. 15, 1999) Vol. 344, No. 3, pp. 731-738. print.
ISSN: 0264-6021.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 29 Mar 2000
Last Updated on STN: 3 Jan 2002
AB The structures of glycosylphosphatidylinositols (GPIs) in Plasmodium have been described (Gerold, Schuppert and Schwarz (1994) J. Biol. Chemical 269, 2597-2606). A detailed understanding of GPI **synthesis** in Plasmodium is a prerequisite for identifying differences present in **biosynthetic** pathways of parasites and host cells. A comparison of the **biosynthetic** pathway of GPIs has revealed differences between mammalian cells and parasitic protozoans. A cell-free incubation system prepared from asexual erythrocytic stages of Plasmodium falciparum, the causative agent of **malaria** in humans, is capable of **synthesizing** the same spectrum of GPIs as that found in metabolically labelled parasites. The formation of mannosylated GPIs in

the cell-free system is shown to be **inhibited** by GTP and, unexpectedly, micromolar concentrations of GDP-Man. Lower concentrations of GDP-Man affect the spectrum of GPIs **synthesized.** The inositol ring of GPIs of P. falciparum is modified by an acyl group. The preferred donor of this **fatty acid** at the inositol ring is myristoyl-CoA. Inositol acylation has to precede the mannosylation of GPIs because, in the absence of acyl-CoA or CoA, mannosylated GPIs were not detected. Inositol myristoylation is a unique feature of plasmodial GPIs and thus might provide a potential **target** for drug therapy.

ED Entered STN: 29 Mar 2000
Last Updated on STN: 3 Jan 2002

CC Biochemistry studies - General 10060
Parasitology - General 60502
Invertebrata: general and systematic - Protozoa 63502

IT Major Concepts
Biochemistry and Molecular Biophysics; Parasitology

IT Chemicals & Biochemicals
glycosylphosphatidylinositol: biosynthesis, mannosylation, potential drug therapy target, structure; inositol: acylation, myristoylation

IT Miscellaneous Descriptors
cell-free incubation system

ORGN Classifier
Sporozoa 35400
Super Taxa
Protozoa; Invertebrata; Animalia
Organism Name
Plasmodium falciparum: parasite
Taxa Notes
Animals, Invertebrates, Microorganisms, Protozoans

RN 87-89-8Q (inositol)
6917-35-7Q (inositol)
173524-45-3Q (INOSITOL)

L181 ANSWER 45 OF 71 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

ACCESSION NUMBER: 2000:70099 BIOSIS
DOCUMENT NUMBER: PREV200000070099
TITLE: Lipid peroxides, nitric oxide and essential fatty acids in patients with Plasmodium falciparum malaria.
AUTHOR(S): Kumar, C. Arun; Das, U. N. [Reprint author]
CORPORATE SOURCE: EFA Sciences, Inc., 1420 Providence Highway, Suite No. 266, Norwood, MA, USA
SOURCE: Prostaglandins Leukotrienes and Essential Fatty Acids, (Oct., 1999) Vol. 61, No. 4, pp. 255-258. print.
CODEN: PLEAEU. ISSN: 0952-3278.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Feb 2000
Last Updated on STN: 3 Jan 2002

AB Long chain polyunsaturated **fatty acids** derived from essential **fatty acids** have been shown to be toxic to Plasmodium falciparum both in vitro and in vivo. Here, we present evidence to suggest that in patients with Plasmodium falciparum **malaria** the levels of lipid peroxides (a marker of free radical **generation**) nitric oxide (a potent free radical with **immunomodulatory** actions), and concentrations of linolenic acid (LA) and alpha-linolenic acid (ALA) are low, whereas those of eicosapentaenoic acid (EPA) are high. The ability of the **fatty acids** to kill P. falciparum is dependent on their capacity to

stimulate free radical **generation** in neutrophils and macrophages. EPA is more potent than LA in killing the parasite. In view of this, the results of the present study suggests that in patients with P. falciparum **malaria** the decreased levels of lipid peroxides and nitric oxide may contribute to the persistence of the infection, whereas elevated levels of EPA may be a feeble attempt to overcome this defect.

ED Entered STN: 16 Feb 2000
Last Updated on STN: 3 Jan 2002

CC Parasitology - General 60502
Biochemistry studies - General 10060
Invertebrata: comparative, experimental morphology, physiology and pathology - Protozoa 64002
Blood - General and methods 15001

IT Major Concepts
Clinical Chemistry (Allied Medical Sciences); Hematology (Human Medicine, Medical Sciences); Parasitology

IT Diseases
malaria: blood and lymphatic disease, parasitic disease
Malaria (MeSH)

IT Chemicals & Biochemicals
alpha-linolenic acid: plasma; eicosapentanoic acid: plasma; linoleic acid: plasma; lipid peroxides: plasma; nitric oxide: plasma

ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human: host, patient
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

ORGN Classifier
Sporozoa 35400
Super Taxa
Protozoa; Invertebrata; Animalia
Organism Name
Plasmodium falciparum: parasite
Taxa Notes
Animals, Invertebrates, Microorganisms, Protozoans

RN 463-40-1 (alpha-linolenic acid)
60-33-3 (linoleic acid)
10102-43-9 (nitric oxide)

L181 ANSWER 46 OF 71 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

ACCESSION NUMBER: 1999:423507 BIOSIS
DOCUMENT NUMBER: PREV199900423507
TITLE: The cloning and expression of pfacs1, a Plasmodium falciparum fatty acyl coenzyme A synthetase-1 targeted to the host erythrocyte cytoplasm.
AUTHOR(S): Matesanz, Fuencisla; Duran-Chica, Isabel; Alcina, Antonio [Reprint author]
CORPORATE SOURCE: Instituto de Parasitologia y Biomedicina "Lopez Neyra" CSIC, Granada, Spain
SOURCE: Journal of Molecular Biology, (Aug. 6, 1999) Vol. 291, No. 1, pp. 59-70. print.
CODEN: JMOBAK. ISSN: 0022-2836.
DOCUMENT TYPE: Article
LANGUAGE: English
OTHER SOURCE: Genbank-AF007828; Genbank-U10121

ENTRY DATE: Entered STN: 18 Oct 1999
Last Updated on STN: 18 Oct 1999

AB Plasmodium is unable to carry out de novo **fatty acid synthesis** and has to obtain these compounds from their host for subsequent activation by thioesterification with coenzyme A. This activity is catalyzed by a fatty acyl-CoA **synthetase** enzyme (EC 6.2.1.3). Here, we describe a novel gene from P. falciparum whose recombinant purified product from baculovirus-transfected insect cell line had the enzymatic activity of a long-chain fatty acyl-CoA **synthetase.** It was named pfacs1, since it belongs to a multi-member gene family as revealed by the sequence of several clones and a multi-band pattern in Southern blots. The sequence specifies a product of 820 amino acid residues. It was transcribed and expressed in infected erythrocytes having an apparent molecular mass of 100 kDa. Immunolabeling of infected erythrocytes with a specific antibody against the carboxy-terminal part of the PfACS1 localized the product early after the erythrocyte invasion in vesicle-like structures budding off the parasitoforous membrane toward the red cell cytoplasm. Its unique carboxy-terminal structure of 70 extra amino acid residues, longer than any other reported acyl-CoA **synthetase**, is probably related to its localization in the cytoplasm of the host erythrocyte. The phylogenetic relationship among other AMP-forming enzymes, placed PfACS1 closer to Saccharomyces cerevisiae, sharing significant amino acid identities, especially in the conserved signature motif that **modulates fatty acid** substrate specificity and ATP/AMP-binding domains. Taking into account the importance of this enzymatic activity for the parasite, its extra-cellular location inside the infected erythrocyte, and the divergence with respect to the homologous human enzymes, it may be an important protein as a potential **target** candidate for chemotherapeutic **antimalaria** drugs.

ED Entered STN: 18 Oct 1999
Last Updated on STN: 18 Oct 1999

CC Enzymes - Chemical and physical 10806
Cytology - Human 02508
Biochemistry studies - Nucleic acids, purines and pyrimidines 10062
Blood - Blood cell studies 15004
Invertebrata: comparative, experimental morphology, physiology and pathology - Protozoa 64002
Tissue culture, apparatus, methods and media 32500
Biophysics - Methods and techniques 10504
Biochemistry studies - Proteins, peptides and amino acids 10064
General biology - Miscellaneous 00532

IT Major Concepts
Enzymology (Biochemistry and Molecular Biophysics); Methods and Techniques

IT Parts, Structures, & Systems of Organisms
erythrocytes: blood and lymphatics

IT Chemicals & Biochemicals
fatty acyl coenzyme A synthetase-1 [Pfacs1] [EC 6.2.1.3]: analysis, cloning, expression; DNA: amplification, cloning, analysis; RNA: isolation

IT Sequence Data
AF007828: Genbank; U10121: Genbank

IT Methods & Equipment
fatty acyl coenzyme A synthetase-1 6His activity assay: activity assays, analytical method; fatty acyl coenzyme A synthetase-1 6His expression vector construction: genetic method, recombinant DNA technology; fatty acyl coenzyme A synthetase-1 6His purification: Isolation/Purification Techniques: CB, purification method; immunoelectron microscopy: microscopy method, scanning electron

microscopy; indirect immunofluorescence assay: Analysis/Characterization Techniques: CB, analytical method; oligonucleotide synthesis: nucleic acid synthesis, synthetic method; parasite erythrocyte culture: cell culture method, cell culture techniques; Applied Biosystems model 381 DNA synthesizer: equipment; Applied Biosystems ABI373 DNA sequencer: equipment; DNA cloning: Recombinant DNA Technology, cloning method; DNA sequence analysis: Analysis/Characterization Techniques: CB, analytical method; Northern blot: detection method, detection/labeling techniques; Perkin Elmer DNA Sequencing Kit: equipment; PCR [polymerase chain reaction]: DNA amplification, DNA amplification method; Southern blot: detection method, detection/labeling techniques; Western blot: detection method, detection/labeling techniques

ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

ORGN Classifier
Sporozoa 35400
Super Taxa
Protozoa; Invertebrata; Animalia
Organism Name
Plasmodium falciparum: strain-3D7
Taxa Notes
Animals, Invertebrates, Microorganisms, Protozoans

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ACCESSION NUMBER: 1998:313401 BIOSIS
DOCUMENT NUMBER: PREV199800313401
TITLE: Synthesis of hydroperoxide and perketal derivatives of polyunsaturated fatty acids as potential antimalarial agents.
AUTHOR(S): Pitt, Michael J.; Easton, Christopher J. [Reprint author]; Robertson, Thomas A.; Kumaratilake, Lakshmi M.; Ferrante, Antonio; Poulos, Alfred; Rathjen, Deborah A.
CORPORATE SOURCE: Res. Sch. Chem., Aust. Natl. Inst., Canberra, ACT 0200, Australia
SOURCE: Tetrahedron Letters, (June 11, 1998) Vol. 39, No. 24, pp. 4401-4404. print.
CODEN: TELEAY. ISSN: 0040-4039.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 22 Jul 1998
Last Updated on STN: 10 Sep 1998

AB Hydroperoxide derivatives of beta-oxa-substituted polyunsaturated **fatty acids** were prepared by 15-lipoxygenase catalysed oxidation and perketal derivatives of **fatty acid** hydroperoxides were **synthesized.** The perketals are more stable than their parent **fatty acid** hydroperoxides, but less active as **antimalarial** agents in the in vitro growth **inhibition** of Plasmodium falciparum.

ED Entered STN: 22 Jul 1998
Last Updated on STN: 10 Sep 1998

CC Biochemistry methods - General 10050
Biochemistry studies - General 10060

Biophysics - General 10502
IT Major Concepts
Methods and Techniques; Pharmaceuticals (Pharmacology)
IT Chemicals & Biochemicals
polyunsaturated fatty acid hydroperoxide perketal derivatives: antimalarial agent, synthesis; polyunsaturated fatty acid hydroperoxides: antimalarial agent, synthesis; polyunsaturated fatty acid: antimalarial agent, hydroperoxide derivative, synthesis, perketal derivative
IT Methods & Equipment
chemical synthesis: synthetic method
RN 14691-59-9 (HYDROPEROXIDE)
14691-59-9D (HYDROPEROXIDE)

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ACCESSION NUMBER: 1997:212809 BIOSIS
DOCUMENT NUMBER: PREV199799519313
TITLE: Signal transduction in macrophages by glycosylphosphatidylinositols of Plasmodium, Trypanosoma, and Leishmania: Activation of protein tyrosine kinases and protein kinase C by inositolglycan and diacylglycerol moieties.
AUTHOR(S): Tachado, Souvenir D. [Reprint author]; Gerold, Peter; Schwarz, Ralph; Novakovic, Suzanna; McConville, Malcolm; Schofield, Louis
CORPORATE SOURCE: Walter Eliza Hall Inst. Med. Res., VIC 3050, Australia
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1997) Vol. 94, No. 8, pp. 4022-4027.
CODEN: PNASA6. ISSN: 0027-8424.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 22 May 1997
Last Updated on STN: 22 May 1997

AB The perturbation of various glycosylphosphatidylinositol (GPI)-anchored surface proteins imparts profound regulatory signals to macrophages, lymphocytes and other cell types. The specific contribution of the GPI moieties to these events however is unclear. This study demonstrates that purified GPIs of Plasmodium falciparum, Trypanosoma brucei, and Leishmania mexicana origin are sufficient to initiate signal transduction when added alone to host cells as chemically defined agonists. GPIs (10 nM-1 mu-M) induce rapid activation of the protein tyrosine kinase (PTK) p59-hck in macrophages. The minimal structural requirement for PTK activation is the evolutionarily conserved core glycan sequence Man-alpha-1-2Man-alpha-1-6Man-alpha-1-4GlcN1-6myo-inositol. GPI-associated diacylglycerols independently activate the calcium-independent epsilon isoform of protein kinase C. Both signals collaborate in regulating the downstream NF-kappa-B/rel-dependent gene expression of interleukin 1-alpha, tumor necrosis factor (TNF) alpha, and inducible NO **synthase.** The alkylacyl-glycerol-containing iM4 GIPL of L. mexicana, however, is unable to activate protein kinase C and **inhibits** TNF expression in response to other agonists, establishing signaling specificity among structurally distinct GPIs. GPI alone appears sufficient to mimic the activities of **malaria** parasite extracts in the signaling pathway leading to TNF expression. A mAb to GPI **blocks** TNF induction by parasite extracts indicating that GPI is a necessary agent in this response. As protozoal GPIs are closely related to their mammalian counterparts, the data indicate that GPIs do indeed constitute a novel outside-in signaling system, acting as both agonists and second messenger

substrates, and imparting at least two separate signals through the structurally distinct glycan and **fatty acid** domains. These activities may underlie aspects of pathology and immune regulation in protozoal infections.

ED Entered STN: 22 May 1997
Last Updated on STN: 22 May 1997

CC Cytology - Animal 02506
Biochemistry studies - Proteins, peptides and amino acids 10064
Biochemistry studies - Lipids 10066
Biochemistry studies - Carbohydrates 10068
Enzymes - Physiological studies 10808
Blood - Blood cell studies 15004
Blood - Lymphatic tissue and reticuloendothelial system 15008
Parasitology - General 60502
Invertebrata: comparative, experimental morphology, physiology and pathology - Protozoa 64002

IT Major Concepts
Biochemistry and Molecular Biophysics; Blood and Lymphatics (Transport and Circulation); Cell Biology; Enzymology (Biochemistry and Molecular Biophysics); Parasitology; Physiology

IT Chemicals & Biochemicals
PROTEIN TYROSINE KINASES; PROTEIN KINASE C

IT Miscellaneous Descriptors
ACTIVATION; BLOOD AND LYMPHATICS; CELL BIOLOGY; ENZYMOLOGY; LEISHMANIA-MEXICANA GLYCOSYLPHOSPHATIDYLINOSITOL; MACROPHAGE; PARASITE; PLASMODIUM-FALCIPARUM GLYCOSYLPHOSPHATIDYLINOSITOL; PROTEIN KINASE C; PROTEIN TYROSINE KINASES; SIGNAL TRANSDUCTION; SIGNAL TRANSDUCTION INITIATOR; STRUCTURE-ACTIVITY RELATIONSHIP; TRYPANOSOMA-BRUCEI GLYCOSYLPHOSPHATIDYLINOSITOL

ORGN Classifier
Flagellata 35200
Super Taxa
Protozoa; Invertebrata; Animalia
Organism Name
Leishmania mexicana
Trypanosoma brucei
Taxa Notes
Animals, Invertebrates, Microorganisms, Protozoans

ORGN Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
RAW 264: cell line
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates

ORGN Classifier
Sporozoa 35400
Super Taxa
Protozoa; Invertebrata; Animalia
Organism Name
Plasmodium falciparum
Taxa Notes
Animals, Invertebrates, Microorganisms, Protozoans

RN 80449-02-1D (PROTEIN TYROSINE KINASES)
141436-78-4 (PROTEIN KINASE C)

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ACCESSION NUMBER: 1997:250901 BIOSIS
DOCUMENT NUMBER: PREV199799550104
TITLE: Odour-mediated, host-seeking behaviour of Anopheles mosquitoes: A new approach.
AUTHOR(S): Knols, B. G. J. [Reprint author]; Takken, W. [Reprint author]; Cork, A.; De Jong, R.
CORPORATE SOURCE: Dep. Entomol., Wageningen Agric. Univ., P.O. Box 8031, 6700 EH Wageningen, Netherlands
SOURCE: Annals of Tropical Medicine and Parasitology, (1997) Vol. 91, No. SUPPL. 1, pp. S117-S118.
CODEN: ATMPA2. ISSN: 0003-4983.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 13 Jun 1997
Last Updated on STN: 13 Jun 1997

AB Investigations of the chemical ecology of host-seeking behaviour of the anthropophilic, **malarial** mosquito Anopheles gambiae s.s. were conducted using observations on biting behaviour, a behavioural bioassay to test the activity of candidate odors, and analytical chemistry of attractive odor mixtures. Anopheles gambiae s.s. landed and bit preferentially on the human foot and it was shown that this behaviour was odor **modulated.** In the bioassay, the mosquitoes were found to be highly attracted to emanations of Limburger cheese, the odors of which are reminiscent of those from human feet. The active compounds in the cheese were found to be **fatty acids** and the mosquitoes were attracted to a **synthetic** mixture of such acids. The ecology of this behaviour is discussed with respect to the odors produced by human skin.

ED Entered STN: 13 Jun 1997
Last Updated on STN: 13 Jun 1997

CC Behavioral biology - Animal behavior 07003
Blood - Blood, lymphatic and reticuloendothelial pathologies 15006
Integumentary system - General and methods 18501
Parasitology - Medical 60504
Invertebrata: comparative, experimental morphology, physiology and pathology - Insecta: physiology 64076

IT Major Concepts
Behavior; Hematology (Human Medicine, Medical Sciences); Integumentary System (Chemical Coordination and Homeostasis); Parasitology; Physiology

IT Miscellaneous Descriptors
BEHAVIOR; BLOOD AND LYMPHATIC DISEASE; HOST-SEEKING BEHAVIOR; INTEGUMENTARY SYSTEM; MALARIA; MALARIAL MOSQUITO; ODOR MEDIATED; PARASITIC DISEASE; PARASITOLOGY; SKIN; VECTOR BIOLOGY

ORGN Classifier
Diptera 75314
Super Taxa
Insecta; Arthropoda; Invertebrata; Animalia
Organism Name
Anopheles gambiae
Taxa Notes
Animals, Arthropods, Insects, Invertebrates

ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

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ACCESSION NUMBER: 1988:158349 BIOSIS
DOCUMENT NUMBER: PREV198885082002; BA85:82002
TITLE: ACYL COENZYME A SYNTHETASE ACTIVITY IN PLASMODIUM-KNOWLESI INFECTED ERYTHROCYTES DISPLAYS PECULIAR SUBSTRATES SPECIFICITIES.
AUTHOR(S): BEAUMELLE B D [Reprint author]; VIAL H J
CORPORATE SOURCE: CNRS UA 530, INSERM U58, 60 RUE DE NAVACELLES, 34100 MONTPELLIER, FRANCE
SOURCE: Biochimica et Biophysica Acta, (1987) Vol. 958, No. 1, pp. 1-9.
CODEN: BBACAQ. ISSN: 0006-3002.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 22 Mar 1988
Last Updated on STN: 22 Mar 1988

AB In its blood stages the **malaria** parasite, Plasmodium, displays very high lipid metabolism. We present evidence for an abundant long-chain acyl-CoA **synthetase** (EC 6.2.1.3) activity in Plasmodium knowlesi-infected simian erythrocytes. The activity was found to be 20-fold higher in the schizont-infected (the last parasite stage) than in control erythrocytes. The cosubstrate requirements of the enzyme were similar to those previously reported for acyl-CoA **synthetases** from other sources. Among the separated reaction products of oleyl-CoA **synthetase**, only PPi and oleyl-CoA were **inhibitory**, with Ki over 350 μM. The **fatty acid** specificity of the parasite acyl-CoA **synthetase** activity was fairly marked and depended on the unsaturation state of the substrate. The tested **fatty acids** displayed similar Vmax, whereas their Km ranged from 11 (palmitate) to 59 μM (arachidonate). Finally, experiments involving heat inactivation and separation on hydroxyapatite excluded the presence of a specific arachidonyl-CoA **synthetase** identical to those present in other cells. On the other hand, **fatty acid** competition experiments evidenced the existence of at least two distinct enzymatic sites for **fatty acid** activation in P. knowlesi-infected simian erythrocytes: one is specific for saturated **fatty acids** and the other for polyunsaturated species, whereas oleate could be activated at both sites.

ED Entered STN: 22 Mar 1988
Last Updated on STN: 22 Mar 1988

CC Cytology - Animal 02506
Biochemistry methods - Lipids 10056
Biochemistry studies - Proteins, peptides and amino acids 10064
Biochemistry studies - Lipids 10066
Enzymes - General and comparative studies: coenzymes 10802
Enzymes - Physiological studies 10808
Metabolism - Lipids 13006
Blood - Blood cell studies 15004
Blood - Blood, lymphatic and reticuloendothelial pathologies 15006
Development and Embryology - General and descriptive 25502
Parasitology - Medical 60504
Invertebrata: comparative, experimental morphology, physiology and pathology - Protozoa 64002

IT Major Concepts
Biochemistry and Molecular Biophysics; Blood and Lymphatics (Transport and Circulation); Development; Enzymology (Biochemistry and Molecular

Biophysics); Metabolism; Parasitology; Physiology
IT Miscellaneous Descriptors
MONKEY EC 6.2.1.3 MALARIA LIPID METABOLISM FATTY ACID ENZYME KINETICS PARASITE DEVELOPMENT
ORGN Classifier
Sporozoa 35400
Super Taxa
Protozoa; Invertebrata; Animalia
Taxa Notes
Animals, Invertebrates, Microorganisms, Protozoans
ORGN Classifier
Cercopithecidae 86205
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Mammals, Nonhuman Vertebrates, Nonhuman Primates, Primates, Vertebrates
RN 9013-18-7 (ACYL COENZYME A SYNTHETASE)
9013-18-7 (EC 6.2.1.3)

L181 ANSWER 51 OF 71 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 1976:171452 BIOSIS
DOCUMENT NUMBER: PREV197662001452; BA62:1452
TITLE: THE IMPORTANCE OF PHOSPHO LIPASE A-2 IN PROSTAGLANDIN BIOSYNTHESIS.
AUTHOR(S): FLOWER R J; BLACKWELL G J
SOURCE: Biochemical Pharmacology, (1976) Vol. 25, No. 3, pp. 285-291.
CODEN: BCPCA6. ISSN: 0006-2952.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: Unavailable
AB A model was devised to examine the cellular biochemical events which culminate in prostaglandin (PG) **biosynthesis** and release from tissues. Slices of guinea-pig spleen incubated in buffer containing [1-14C]arachidonic acid incorporate the label into cellular phospholipid and neutral lipid pools. The majority of incorporated radioactivity appeared in the lecithin fraction: smaller amounts were associated with neutral lipids (chiefly diglycerides) or remained unesterified. During incubation there was a small basal release of prostaglandins. When tissues were vibrated mechanically or shocked there was a loss of [1-14C]arachidonic acid from the phospholipid pools, a corresponding rise in the free substrate levels and an increase in the **synthesis** of 14C-labeled PGestradiol(E2). The **synthesis** of prostaglandins was **blocked** by indomethacin, and the loss of arachidonate from the phospholipid fraction of the cells was **blocked** by the anti-**malarial** drug mepacrine. During mechanical vibration or immunological challenge the labeled arachidonic acid released as a substrate for prostaglandin **biosynthesis** originated solely from the phospholipid fraction. Phospholipase is the key enzyme which mobilizes free **fatty acids** for prostaglandin **biosynthesis** during these types of cell injury. Spleen slices were also vibrated in the presence of labeled arachidonic acid without prior incorporation. This procedure increased prostaglandin **biosynthesis** several-fold, indicating that substrate availability is not the only requirement for stimulation of prostaglandin **biosynthesis.**
CC Cytology - Animal 02506
Radiation biology - Radiation and isotope techniques 06504

Comparative biochemistry 10010
Biochemistry methods - Lipids 10056
Biochemistry studies - General 10060
Biochemistry studies - Proteins, peptides and amino acids 10064
Biochemistry studies - Lipids 10066
Biophysics - Methods and techniques 10504
External effects - Electric, magnetic and gravitational phenomena 10610
External effects - Physical and mechanical effect 10612
Enzymes - Chemical and physical 10806
Metabolism - General metabolism and metabolic pathways 13002
Metabolism - Lipids 13006
Metabolism - Proteins, peptides and amino acids 13012
Blood - Lymphatic tissue and reticuloendothelial system 15008
Endocrine - General 17002
Pharmacology - Drug metabolism and metabolic stimulators 22003
In vitro cellular and subcellular studies 32600
Immunology - General and methods 34502
Chemotherapy - Antiparasitic agents 38510

IT Major Concepts
Biochemistry and Molecular Biophysics; Blood and Lymphatics (Transport and Circulation); Cell Biology; Endocrine System (Chemical Coordination and Homeostasis); Enzymology (Biochemistry and Molecular Biophysics); Metabolism; Pharmacology

IT Miscellaneous Descriptors
GUINEA-PIG SPLEEN INDOMETHACIN MEPACRINE METAB-DRUGS LECITHIN ARACHIDONIC-ACID

ORGN Classifier
Caviidae 86300
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates

RN 9001-84-7 (PHOSPHOLIPASE-A2)
53-86-1 (INDOMETHACIN)
83-89-6 (MEPACRINE)
506-32-1 (ARACHIDONIC-ACID)

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on STN DUPLICATE 6

ACCESSION NUMBER: 2001245232 EMBASE
TITLE: Bacterial **fatty-acid biosynthesis**: An antibacterial drug **target** waiting to be exploited.
AUTHOR: Heath R.J.
CORPORATE SOURCE: R.J. Heath, Protein Production Facility, St Jude Children's Hospital, Memphis, TN, United States
SOURCE: Drug Discovery Today, (1 Jul 2001) 6/14 (715).
Refs: 8
ISSN: 1359-6446 CODEN: DDTOFS
PUBLISHER IDENT.: S 1359-6446(01)01881-5
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Note
FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index
004 Microbiology
LANGUAGE: English
CT Medical Descriptors:
*fatty acid synthesis
*Escherichia coli

drug development
drug mechanism
enzyme inhibition
Mycobacterium
Bacillus subtilis
gene overexpression
Plasmodium falciparum
note
Drug Descriptors:
*antiinfective agent: PD, pharmacology
*antiinfective agent: DV, drug development
*antiinfective agent: CM, drug comparison
*fatty acid synthase: EC, endogenous compound
*enzyme inhibitor: PD, pharmacology
*enzyme inhibitor: DV, drug development
*enzyme inhibitor: CM, drug comparison
***antimalarial agent: PD, pharmacology**
***antimalarial agent: DV, drug development**
***antimalarial agent: CM, drug comparison**
triclosan: PD, pharmacology
triclosan: CM, drug comparison
isoniazid: PD, pharmacology
isoniazid: CM, drug comparison
cerulenin: PD, pharmacology
cerulenin: DV, drug development
cerulenin: CM, drug comparison
thiolactomycin: PD, pharmacology
thiolactomycin: DV, drug development
thiolactomycin: CM, drug comparison
boron derivative: PD, pharmacology
boron derivative: DV, drug development
boron derivative: CM, drug comparison
boron derivative: AN, drug analysis
carrier protein: EC, endogenous compound
oxidoreductase: EC, endogenous compound
isoenzyme: EC, endogenous compound
flavoprotein: EC, endogenous compound
diazaborine derivative: PD, pharmacology
diazaborine derivative: DV, drug development
diazaborine derivative: CM, drug comparison
diazaborine derivative: AN, drug analysis
unclassified drug
RN (fatty acid synthase) 9045-77-6; (**triclosan**) **3380-34-5** ; (isoniazid) 54-85-3, 62229-51-0, 65979-32-0; (**cerulenin**) **17397-89-6**; (thiolactomycin) 82079-32-1; (carrier protein) 80700-39-6; (oxidoreductase) 9035-73-8, 9035-82-9, 9037-80-3, 9055-15-6

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on STN DUPLICATE 7
ACCESSION NUMBER: 2001221109 EMBASE
TITLE: Brave new world of post-genomics!.
AUTHOR: Fairlamb A.H.
CORPORATE SOURCE: A.H. Fairlamb, Division of Biological Chemistry, Wellcome Trust Biocentre, University of Dundee, Dundee DD1 5EH, United Kingdom. a.h.fairlamb@dundee.ac.uk
SOURCE: Trends in Parasitology, (2001) 17/6 (255-256).
Refs: 10
ISSN: 1471-4922 CODEN: TPRACT
PUBLISHER IDENT.: S 1471-4922(01)01977-8
COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 004 Microbiology
037 Drug Literature Index
LANGUAGE: English
CT Medical Descriptors:
*Saccharomyces cerevisiae
*Haemophilus influenzae
*Neisseria meningitidis
*Trypanosoma
*Mycobacterium tuberculosis
*Leishmania
gene sequence
bacterial virulence
parasite virulence
gene
information retrieval
data base
DNA microarray
gene expression
gene function
expressed sequence tag
malaria
fatty acid synthesis
human
nonhuman
conference paper
Drug Descriptors:
antigen: EC, endogenous compound
gene product: EC, endogenous compound
trypanothione: EC, endogenous compound
ovothiol A: EC, endogenous compound
mycothiol: EC, endogenous compound
thiol derivative: EC, endogenous compound
lipophosphoglycan: EC, endogenous compound
fosmidomycin
triclosan
vaccine
unclassified drug
RN (trypanothione) 96304-42-6; (ovothiol A) 108418-13-9; (thiol derivative) 13940-21-1; (fosmidomycin) 66508-37-0, 66508-53-0; (**triclosan**) **3380-34-5**

L181 ANSWER 54 OF 71 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
ACCESSION NUMBER: 2001064504 EMBASE
TITLE: New agents to combat **malaria.**
AUTHOR: Beeson J.G.; Winstanley P.A.; McFadden G.I.; Brown G.V.
CORPORATE SOURCE: J.G. Beeson, Department of Medicine, University of Melbourne, Royal Melbourne Hospital, Victoria, Australia. beeson@unimelb.edu.au
SOURCE: Nature Medicine, (2001) 7/2 (149-150).
Refs: 9
ISSN: 1078-8956 CODEN: NAMEFI
COUNTRY: United States
DOCUMENT TYPE: Journal; (Short Survey)
FILE SEGMENT: 030 Pharmacology
036 Health Policy, Economics and Management
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB **Triclosan**, an antibacterial agent found in mouthwashes, acne medicines and deodorants, also prevents the growth of Plasmodium falciparum. If properly developed, this type II **fatty acid biosynthesis inhibitor** may be a promising new **antimalarial** agent.

CT Medical Descriptors:
***malaria: DM, disease management**
***malaria: DR, drug resistance**
***malaria: DT, drug therapy**
Plasmodium falciparum
antibacterial activity
drug mechanism
drug efficacy
drug cost
human
human tissue
human cell
short survey
priority journal
Drug Descriptors:
***triclosan: CM, drug comparison**
***triclosan: DV, drug development**
***triclosan: DT, drug therapy**
***triclosan: PE, pharmacoeconomics**
***triclosan: PD, pharmacology**
***antimalarial agent: CM, drug comparison**
***antimalarial agent: DV, drug development**
***antimalarial agent: DT, drug therapy**
***antimalarial agent: PE, pharmacoeconomics**
***antimalarial agent: PD, pharmacology**
*thiolactomycin: PD, pharmacology
***fatty acid synthesis inhibitor**
chloroquine: DT, drug therapy
chloroquine: PD, pharmacology
fansidar: DT, drug therapy
fansidar: PD, pharmacology
quinine: DT, drug therapy
quinine: PD, pharmacology
mefloquine: DT, drug therapy
mefloquine: PD, pharmacology
halofantrine: DT, drug therapy
halofantrine: PD, pharmacology
atovaquone: DT, drug therapy
atovaquone: PD, pharmacology
proguanil: DT, drug therapy
proguanil: PD, pharmacology
artemether: DT, drug therapy
artemether: PD, pharmacology
benflumetol: DT, drug therapy
benflumetol: PD, pharmacology
unclassified drug

RN (**triclosan**) **3380-34-5**; (thiolactomycin) 82079-32-1; (chloroquine) 132-73-0, 3545-67-3, 50-63-5, 54-05-7; (fansidar) 37338-39-9; (quinine) 130-89-2, 130-95-0, 14358-44-2, 549-48-4, 549-49-5, 60-93-5, 7549-43-1; (mefloquine) 51773-92-3, 53230-10-7; (halofantrine) 36167-63-2, 66051-63-6, 66051-74-9, 66051-76-1, 69756-53-2; (atovaquone) 94015-53-9, 95233-18-4; (proguanil) 500-92-5, 637-32-1; (artemether) 71963-77-4; (benflumetol) 82186-77-4

L181 ANSWER 55 OF 71 EMBASE

on STN
ACCESSION NUMBER: 2001414148 EMBASE
TITLE: The apicoplast as an **antimalarial** drug target.
AUTHOR: Ralph S.A.; D'Ombrain M.C.; McFadden G.I.
CORPORATE SOURCE: G.I. McFadden, Plant Cell Biology Research Centre, School of Botany, University of Melbourne, Melbourne, Vic. 3010, Australia. g.mcfadden@botany.unimelb.edu.au
SOURCE: Drug Resistance Updates, (2001) 4/3 (145-151).
Refs: 71
ISSN: 1368-7646 CODEN: DRUPFW
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; (Short Survey)
FILE SEGMENT: 004 Microbiology
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Resistance to commonly used **malaria** drugs is spreading and new drugs are required urgently. The recent identification of a relict chloroplast (apicoplast) in **malaria** and related parasites offers numerous new targets for drug therapy using well-characterized compounds. The apicoplast contains a range of metabolic pathways and housekeeping processes that differ radically to those of the host thereby presenting ideal strategies for drug therapy. Indeed, many compounds targeting these plastid pathways are **antimalarial** and have favourable profiles based on extensive knowledge from their use as antibacterials. .COPYRGT. 2001 Harcourt Publishers Ltd.

CT Medical Descriptors:
*apicoplast
*chloroplast
***malaria: DR, drug resistance**
***malaria: DT, drug therapy**
***malaria: ET, etiology**
drug targeting
cell metabolism
antiprotozoal activity
plastid
Plasmodium falciparum
DNA replication
DNA transcription
RNA translation
fatty acid synthesis
amino acid synthesis
heme synthesis
drug induced disease: SI, side effect
human
short survey
priority journal
Drug Descriptors:
***antimalarial agent: AE, adverse drug reaction**
***antimalarial agent: DT, drug therapy**
***antimalarial agent: PD, pharmacology**
antiinfective agent: AE, adverse drug reaction
antiinfective agent: DT, drug therapy
antiinfective agent: PD, pharmacology
ciprofloxacin: AE, adverse drug reaction
ciprofloxacin: DT, drug therapy
ciprofloxacin: PD, pharmacology
rifampicin: DT, drug therapy

rifampicin: PD, pharmacology
clindamycin: DT, drug therapy
clindamycin: PD, pharmacology
erythromycin: DT, drug therapy
erythromycin: PD, pharmacology
azithromycin: DT, drug therapy
azithromycin: PD, pharmacology
spiramycin: DT, drug therapy
spiramycin: PD, pharmacology
thiostrepton: DT, drug therapy
thiostrepton: PD, pharmacology
micrococcin: DT, drug therapy
micrococcin: PD, pharmacology
chloramphenicol: DT, drug therapy
chloramphenicol: PD, pharmacology
doxycycline: DT, drug therapy
doxycycline: PD, pharmacology
tetracycline: DT, drug therapy
tetracycline: PD, pharmacology
amythiamicin: DT, drug therapy
amythiamicin: PD, pharmacology
glyphosate: DT, drug therapy
glyphosate: PD, pharmacology
fosmidomycin: DT, drug therapy
fosmidomycin: PD, pharmacology
thiolactomycin: DT, drug therapy
thiolactomycin: PD, pharmacology
clodinafop: DT, drug therapy
clodinafop: PD, pharmacology
quizalofop: DT, drug therapy
quizalofop: PD, pharmacology
haloxyfop: DT, drug therapy
haloxyfop: PD, pharmacology
triclosan: AE, adverse drug reaction
triclosan: DT, drug therapy
triclosan: PD, pharmacology
quinolone derivative: DT, drug therapy
quinolone derivative: PD, pharmacology
quinoline derived antiinfective agent: DT, drug therapy
quinoline derived antiinfective agent: PD, pharmacology
isoniazid
tuberculostatic agent
unclassified drug

RN (ciprofloxacin) 85721-33-1; (rifampicin) 13292-46-1; (clindamycin) 18323-44-9; (erythromycin) 114-07-8, 70536-18-4; (azithromycin) 83905-01-5; (spiramycin) 8025-81-8; (thiostrepton) 1393-48-2; (micrococcin) 1392-45-6; (chloramphenicol) 134-90-7, 2787-09-9, 56-75-7; (doxycycline) 10592-13-9, 17086-28-1, 564-25-0; (tetracycline) 23843-90-5, 60-54-8, 64-75-5; (glyphosate) 1071-83-6; (fosmidomycin) 66508-37-0, 66508-53-0; (thiolactomycin) 82079-32-1; (haloxyfop) 69806-34-4; (**triclosan**) **3380-34-5**; (isoniazid) 54-85-3, 62229-51-0, 65979-32-0

L181 ANSWER 56 OF 71 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 87054923 EMBASE
DOCUMENT NUMBER: 1987054923
TITLE: Inhibition of melanin biosynthesis by **cerulenin** in appressoria of Colletotrichum lagenarium.
AUTHOR: Kubo Y.; Katoh M.; Furusawa I.; Shishiyama J.

CORPORATE SOURCE: Laboratory of Plant Pathology, Faculty of Agriculture, Kyoto University, Kyoto 606, Japan
SOURCE: Experimental Mycology, (1986) 10/4 (301-306). CODEN: EXMYD2
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
004 Microbiology
LANGUAGE: English
CT Medical Descriptors:
*drug efficacy
*drug inhibition
*drug mechanism
*fungus
***malaria**
*scytalone
drug administration
preliminary communication
nonhuman
in vitro study
Drug Descriptors:
***cerulenin**
*melanin
RN (**cerulenin**) **17397-89-6**; (melanin) 8049-97-6
CO Sigma

=> d iall abeq tech abex 57-58
YOU HAVE REQUESTED DATA FROM FILE 'WPIX, HCAPLUS, MEDLINE, EMBASE, BIOSIS, BIOTECHDS, BIOTECHNO, DRUGU' - CONTINUE? (Y)/N:y

L181 ANSWER 57 OF 71 WPIX COPYRIGHT 2004 THE THOMSON CORP on STN
ACCESSION NUMBER: 2002-154688 [20] WPIX
DOC. NO. CPI: C2002-048364
TITLE: New 1-aryl-5-(2,6-dichloro-benzyloxy)indan-2-carboxylic **acid** derivatives are **fatty acid synthase inhibitors** used for treating bacterial infections.
DERWENT CLASS: B05
INVENTOR(S): CHRISTENSEN, S B; MERCER, D J; XIANG, J
PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP
COUNTRY COUNT: 96
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2002002119	A1	20020110	(200220)*	EN	22	A61K031-50
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW						
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW						
AU 2001071718	A	20020114	(200237)			A61K031-50

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE

WO 2002002119	A1	WO 2001-US20926	20010629
AU 2001071718	A	AU 2001-71718	20010629

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2001071718	A	Based on	WO 2002002119

PRIORITY APPLN. INFO: US 2000-214889P 20000629
INT. PATENT CLASSIF.:
MAIN: A61K031-50
SECONDARY: A61K031-18; C07C315-00; C07C321-00; C07D231-02
BASIC ABSTRACT:
WO 200202119 A UPAB: 20020402
NOVELTY - 1-Aryl-5-(2,6-dichloro-benzyloxy)indan-2-carboxylic acid derivatives (I) are new.
DETAILED DESCRIPTION - 1-Aryl-5-(2,6-dichloro-benzyloxy)indan-2-carboxylic acid derivatives of formula (I) and their salts and salt complexes, are new.
R = OH or RbSO2NH;
Rb = alkyl or Ar (optionally substituted by 1-3 Q);
Ar = Ph, pyridinyl, pyrimidinyl or thiophenyl (all optionally substituted by 1-3 Q);
Q = alkyl, 1-4C alkoxy, Cl, Br, F, methylenedioxy, CN or CO2Rc;
Ra = OH, Cl, Br, F, alkyl, 1-3C alkoxy, NH2, CO2H, CN or OH-Cl2-alkyl, and
Rc = H or alkyl.
An INDEPENDENT CLAIM is also included for the preparation of (I).
ACTIVITY - Antibacterial; Protozoacide; Tuberculostatic.
MECHANISM OF ACTION - **Fatty acid synthase inhibitor.**
Tests are described, but no results are given.
USE - Used for treating bacterial infections (claimed), particularly gram positive and gram negative bacterial infections having a type II fatty acid synthesis pathway, malaria and tuberculosis.
Dwg.0/0
FILE SEGMENT: CPI
FIELD AVAILABILITY: AB; GI; DCN
MANUAL CODES: CPI: B06-A02; B06-H; B07-B01; B07-D04B; B07-D04C; B07-D12; B07-H; B10-A08; B10-A15; B10-B01A; B10-B02A; B10-C02; B10-C04A; B14-A01; B14-A01B1; **B14-A03B**; B14-D06
TECH UPTX: 20020402
TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation: Preparation of (I) comprises reduction of a beta-ketoester compound of formula (II) with a reducing agent in a solvent.
ABEX UPTX: 20020402
SPECIFIC COMPOUNDS - 8 Compounds (I) are specifically e.g: 1-(6-Chloro-benzo(1,3)dioxol-5-yl)-5-(2,6-dichloro-benzyloxy)-indan-2-carboxylic acid (Ia).

ADMINISTRATION - The dosage is 1-140 mg/kg orally, topically or parenterally.
EXAMPLE - To 1-(6-Chloro-benzo(1,3)dioxol-5-yl)-5-(2,6-dichloro-benzyloxy)-3-oxo-indan-2-carboxylic acid methyl ester (55 mg) in trifluoroacetic acid (TFA) (1 ml) was added sodium cyanoborohydride (33 mg) and stirred at room temperature for 24 hours. After removing the TFA, saturated potassium carbonate solution was added and the resulting mixture was extracted with

1:1 mixture of hexane/ethyl acetate followed by basic work-up to give 1-(6-chloro-benzo(1,3)dioxol-5-yl)-5-(2,6-dichloro-benzyloxy)-indan-2-carboxylic acid methyl ester (0.049 g; 46% yield).
To a solution of this compound (508 mg) in tetrahydrofuran (7.5 ml) and water (2.5 ml) was added lithium hydroxide monohydrate (210 mg). The resulting solution was stirred at room temperature overnight. The solution was acidified with 1 N hydrochloric acid and the mixture was extracted with EtOAc, followed by basic work-up to give 1-(6-chloro-benzo(1,3)dioxol-5-yl)-5-(2,6-dichloro-benzyloxy)-indan-2-carboxylic acid (0.1 g, 20% yield).
To a solution of (III) (67 mg) in THF (1.5 ml) was added oxalyl chloride (115 micro-l) and catalytic amount of DMF (2 micro-l). The resulting mixture was stirred at room temperature for 90 minutes. The solvent was then evaporated and the crude 1-(6-chloro-benzo(1,3)dioxol-5-yl)-5-(2,6-dichloro-benzyloxy)-indan-2-carbonyl chloride was used for the further reaction.
To this compound (79 mg) in dichloromethane was added DMAP (27 mg) and methanesulfonamide (21 mg). The resulting solution was stirred at room temperature under argon for five hours. The reaction was quenched with 1 N hydrochloric acid and the mixture was extracted with ethyl acetate followed by basic work up to give N-(1-(1-(6-chlorobenzo(1,3)dioxol-5-yl)-5-(2,6-dichloro-benzyloxy)-3-oxo-indan-2-yl)-methanoyl)-methanesulfonamide (0.055 g; 65% yield).

L181 ANSWER 58 OF 71 WPIX COPYRIGHT 2004 THE THOMSON CORP on STN
ACCESSION NUMBER: 2002-130864 [17] WPIX
DOC. NO. CPI: C2002-040242
TITLE: New indole derivatives useful for treating gram positive or gram negative bacterial infection of an animal e.g. human.
DERWENT CLASS: B02
INVENTOR(S): CHRISTENSEN, S B; DAINES, R A; HEAD, M S; LEBER, J D
PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP
COUNTRY COUNT: 96
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2002000620	A1	20020103	(200217)*	EN	17	C07D209-08
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW						
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW						
AU 2001071531	A	20020108	(200235)			C07D209-08
US 6670388	B1	20031230	(200402)			A61K031-405

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002000620	A1	WO 2001-US20475	20010627
AU 2001071531	A	AU 2001-71531	20010627
US 6670388	B1 Provisional	US 2000-214586P	20000627
		WO 2001-US20475	20010627
		US 2002-296775	20021213

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2001071531	A Based on	WO 2002000620
US 6670388	B1 Based on	WO 2002000620

PRIORITY APPLN. INFO: US 2000-214586P 20000627; US 2002-296775 20021213

INT. PATENT CLASSIF.:
MAIN: A61K031-405; C07D209-08
SECONDARY: A61P043-00

BASIC ABSTRACT:

WO 200200620 A UPAB: 20020313

NOVELTY - Indole derivatives are new.

DETAILED DESCRIPTION - An indole derivative of formula (I) or its salt or salt complex is new.

R = optionally substituted (hetero)aryl; and

n = 0 - 6.

ACTIVITY - Antibacterial; tuberculostatic; protozoacide.

MECHANISM OF ACTION - beta -Ketoacyl-acyl carrier protein (ACP) synthase (FabH) inhibitor. Test details are described but no results given.

USE - For treating bacterial infections (claimed) such as gram positive and gram negative bacterial infections of animal e.g. human; as **fatty acid synthase** (FabH) **inhibitors**; useful as antibiotics; for treating any disease caused by pathogens possessing a type II fatty acid synthesis pathway such as mycobacteria e.g. malaria and tuberculosis. The gram-negative bacteria includes Escherichia coli and Klebsiella pneumoniae and gram positive bacteria includes Staphylococcus aureus, Streptococcus pneumoniae, Enterococcus faecalis and Enterococcus faecium.

ADVANTAGE - The compound is a potentially broad-spectrum **target** against **fatty acid biosynthesis**

Dwg.0/0

FILE SEGMENT: CPI
FIELD AVAILABILITY: AB; GI; DCN
MANUAL CODES: CPI: B06-A02; B06-D01; B07-B01; B14-A01; B14-A01B1; B14-A03; **B14-A03B**; B14-D08; B14-D10

ABEX UPTX: 20020313

SPECIFIC COMPOUNDS - 5-(2-Chloro-5-hydroxybenzyloxy)-1-((2-thiophen-3-yl)ethyl)-1H-indole-2-carboxylic acid and 1-((6-chlorobenzo(1,3)dioxol-5-yl)methyl)-5-(2-chloro-5-hydroxybenzyloxy)-1H-indole-2-carboxylic acid are specifically claimed as (I).

ADMINISTRATION - The composition comprising the compound is administered orally, topically or parenterally (including intravenously, intramuscularly or intraperitoneally) in a unit dosage of 50 - 500 mg. The dosage administered for adult human is 1 - 140 mg/kg body weight.

EXAMPLE - To a solution of 4-chloro-3-methylphenol (1 g) in dry CH2Cl2 (70 ml) at 0 degreesC was added Et3N (1.45 ml). After stirring at 0 degreesC for 20 minutes benzenesulfonyl chloride (1.34 ml) was added to the reaction mixture. The solution was warmed and after basic workup gave benzenesulfonic acid 4-chloro-3-methylphenyl ester (a). To a solution of (a) (0.5 g) in CCl4 (10 ml) was added N-bromosuccinamide (0.38 g). The mixture after basic workup gave benzenesulfonic acid-3-bromomethyl-4-chlorophenylester (b). To a solution of 5-hydroxyindole-2-carboxylic acid ethyl ester (14.2 g) (prepared from 5-benzyloxyindole-2-carboxylic acid ethyl ester (10 g) in ethanol) in DMF (dimethylformamide) (150 ml) was added cesium carbonate (26.8 g). The mixture after further workup gave 5-allyloxyindole-2-carboxylic acid ethyl ester (c). To a solution of (c)

(1 g) in THF (tetrahydrofuran) (10 ml) was added azodicarboxylic acid bis(dimethylamide) (TMAD; 1.4 g). The mixture, after further basic workup gave 5-allyloxy-1-((2-thiophen-3-yl)ethyl)-1H-indole-2-carboxylic acid ethyl ester (d). To (d) (1.36 g) was added a mixture of dichloromethane:morpholine:water (100:10:2, 50 ml) followed by addition of tetrakis (triphenylphosphine) palladium(O) (300 mg). After basic workup, the reaction mixture gave 5-hydroxy-1-((2-thiophen-3-yl)ethyl)-1H-indole-2-carboxylic acid ethyl ester (e). To a solution of (e) (0.42 g) in dry DMF (10 ml) was added Cs2CO3 (0.65 g) and after basic workup gave 5-(5-benzenesulfonyloxy-2-chlorobenzyloxy)-1-((2-thiophen-3-yl)ethyl)-1H-indole-2-carboxylic acid ethyl ester (f). (f) (1 g) was dissolved in mixed solvent (THF:EtOH:H2O, (2:2:1, 15 ml)). To this solution was added NaOH (1N, 2.5 ml) and stirred. After further workup the reaction mixture gave 5-(2-chloro-5-hydroxybenzyloxy)-1-((2-thiophen-3-yl)ethyl)-1H-indole-2-carboxylic acid (g).

=> d ibib abs ed 59
YOU HAVE REQUESTED DATA FROM FILE 'WPIX, HCAPLUS, MEDLINE, EMBASE, BIOSIS, BIOTECHDS, BIOTECHNO, DRUGU' - CONTINUE? (Y)/N:y

'ED' IS NOT A VALID FORMAT
In a multifile environment, a format can only be used if it is valid in at least one of the files. Refer to file specific help messages or the STNGUIDE file for information on formats available in individual files.
REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):ibib abs

L181 ANSWER 59 OF 71 BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2004-09656 BIOTECHDS
TITLE: New Fab I enzyme enoyl acyl carrier protein reductase (ENR) from Toxoplasma gondii, useful for developing antimicrobial agents, or inhibitors of apicomplexan growth and survival; involving vector-mediated gene transfer and expression in host cell for use in gene targeting and inhibitor, antimicrobial and antibacterial agent preparation
AUTHOR: MCLEOD R L; MUI E J; SAMUEL B U; MACK D G; KIRISITS M J; WENDER P; ROTHBARD J; HEARN B; ROBERTS C W; RICE D W; MUENCH S P; PRIGGE S; CAMPBELL S A; COGGINS J R; ROBERTS F; HENRIQUEZ F L; MILHOUS W K; KYLE D E
PATENT ASSIGNEE: MCLEOD R L; MUI E J; SAMUEL B U; MACK D G; KIRISITS M J; WENDER P; ROTHBARD J; HEARN B; ROBERTS C W; RICE D W; MUENCH S P; PRIGGE S; CAMPBELL S A; COGGINS J R; ROBERTS F; HENRIQUEZ F L; MILHOUS W K; KYLE D E
PATENT INFO: WO 2004016220 26 Feb 2004
APPLICATION INFO: WO 2003-US25571 14 Aug 2003
PRIORITY INFO: US 2003-472887 23 May 2003; US 2002-404033 15 Aug 2002
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2004-192063 [18]
AN 2004-09656 BIOTECHDS
AB DERWENT ABSTRACT:
NOVELTY - A molecule of the Fab I enzyme comprising the amino acid sequence of the Fab I enzyme in Toxoplasma gondii consisting of 417 amino acids (I), or an amino acid sequence that is substantially similar and has the same function, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for: (1) an isolated DNA molecule encoding T. gondii enoyl acyl carrier protein reductase (ENR), or comprising a sequence of 3462 base pairs (bp), as

given in the specification; (2) a recombinant T. gondii ENR; (3) a molecule of the DAHP (D-arabino-heptulosonate-7-phosphate) synthase gene encoding a 544 amino acid sequence of the enzyme in T. gondii; (4) a crystal preparation of Plasmodium falciparum ENR (Fabl); (5) a novel recombinant protein with an amino acid sequence substantially similar to that of T. gondii sequence (I), and having the same function; (6) delivering a pharmaceutical composition into a microorganism by attaching at least one polypeptide to the composition to form a complex and contacting the microorganism with the polypeptide composition complex; and (7) testing a candidate transporter for delivery of a pharmaceutical composition into a microorganism by contacting the pharmaceutical composition with the candidate transporter, and determining whether the pharmaceutical composition is delivered into the microorganism by the candidate transporter.

BIOTECHNOLOGY - Preferred Method: In delivering a pharmaceutical composition to a microorganism, the microorganism is a parasite, particularly Toxoplasma gondii. The polypeptide is polyarginine, specifically octaarginine. The composition is delivered to the encysted T. gondii bradyzoites. The composition is a small molecule or **triclosan.**

ACTIVITY - Antibacterial; Antimicrobial; Antiparasitic. No biological data given.

MECHANISM OF ACTION - Vaccine. No biological data given.

USE - The amino acid sequence information from apicomplexan Fab I (particularly of T. gondii) or DAHP (D-arabino-heptulosonate-7-phosphate) synthase is useful as a target for developing inhibitors and antimicrobial agents against disease causing agents, such as bacteria. The recombinant protein is useful in determining the crystal structure of the enzyme from which novel inhibitors can be designed. The information on the mRNA sequence corresponding to the amino acid sequence of apicomplexan Fab I can be used to develop interfering RNA which will compete for the FAB I mRNA. The plastid targeting sequence of the Toxoplasma gondii Fab I amino acid sequence may be used to design antimicrobial agents and inhibitors of apicomplexan growth and survival. **Triclosan** are useful for inhibiting apicomplexan growth and survival (all claimed).

EXAMPLE - A cDNA library was screened to identify and characterize T. gondii enoyl acyl carrier protein reductase (ENR) gene. cDNA library was constructed using tachyzoites of the RH strain of T. gondii. A genomic DNA sequence containing a portion of the 3' end of the T. gondii ENR gene was identified by searching the T. gondii DNA database with ENR DNA sequences from **malarial** parasites. An amino acid sequence of the 3' end of T. gondii ENR was deduced from this genomic DNA and compared with other ENR sequences including Brassica napus, Escherichia coli and Plasmodium falciparum . PCR primers were designed and used to amplify a portion of the 3' end of the target gene using genomic DNA from the RH strain of T. gondii as the PCR template. The T. gondii ENR probe was used to identify 6 clones that were isolated from the T. gondii cDNA library. Analysis of the sequences derived from the 6 clones revealed that 4 of the clones contained the entire cDNA sequence and that 2 of the clones contained only partial sequence of T. gondii ENR. The largest cDNA ENR clone contained 3462 nucleotides. The amino acid sequence of the T. gondii ENR was deduced by translation of the sequence and revealed that there are 417 amino acids in the putative protein. (129 pages)

=> d ibib abs 60-71
YOU HAVE REQUESTED DATA FROM FILE 'WPIX, HCAPLUS, MEDLINE, EMBASE, BIOSIS, BIOTECHDS, BIOTECHNO, DRUGU' - CONTINUE? (Y)/N:y

L181 ANSWER 60 OF 71 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
ACCESSION NUMBER: 2003:37432708 BIOTECHNO
TITLE: Identification, Characterization, and Inhibition of Plasmodium falciparum β-Hydroxyacyl-Acyl Carrier Protein Dehydratase (FabZ)
AUTHOR: Sharma S.K.; Kapoor M.; Ramya T.N.C.; Kumar S.; Kumar G.; Modak R.; Sharma S.; Surolia N.; Surolia A.
CORPORATE SOURCE: N. Surolia, Molecular Biology and Genetics Unit, Jawaharlal Nehru Ctr. Adv. Sci. Res., Jakkur, Bangalore 560064, India.
E-mail: surolia@jncasr.ac.in
SOURCE: Journal of Biological Chemistry, (14 NOV 2003), 278/46 (45661-45671), 47 reference(s)
CODEN: JBCHA3 ISSN: 0021-9258
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 2003:37432708 BIOTECHNO
AB The emergence of drug-resistant forms of Plasmodium falciparum emphasizes the need to develop new **antimalarials.** In this context, the fatty acid biosynthesis (FAS) pathway of the **malarial** parasite has recently received a lot of attention. Due to differences in the fatty acid biosynthesis systems of Plasmodium and man, this pathway is a good target for the development of new and selective therapeutic drugs directed against **malaria.** In continuation of these efforts we report cloning and overexpression of P. falciparum β-hydroxyacyl-acyl carrier protein (ACP) dehydratase (PffabZ) gene that codes for a 17-kDa protein. The enzyme catalyzes the dehydration of β-hydroxyacyl-ACP to trans-2-acyl-ACP, the third step in the elongation phase of the FAS cycle. It has a K.sub.m of 199 μM and k .sub.c.sub.a.sub.t/K.sub.m of 80.4 M.sup.-.sup.1 s.sup.-.sup.1 for the substrate analog β-hydroxybutyryl-CoA but utilizes crotonoyl-CoA, the product of the reaction, more efficiently (K.sub.m = 86 μM, k .sub.c.sub.a.sub.t/ K.sub.m = 220 M.sup.-.sup.1 s.sup.-.sup.1). More importantly, we also identify inhibitors (NAS-91 and NAS-21) for the enzyme. Both the inhibitors prevented the binding of crotonoyl-CoA to PfFabZ in a competitive fashion. Indeed these inhibitors compromised the growth of P. falciparum in cultures and **inhibited** the parasite **fatty acid synthesis** pathway both in cell-free extracts as well as in situ. We modeled the structure of PfFabZ using Escherichia coli β-hydroxydecanoyl thioester dehydratase (EcFabA) as a template. We also modeled the inhibitor complexes of PfFabZ to elucidate the mode of binding of these compounds to FabZ. The discovery of the inhibitors of FabZ, reported for the first time against any member of this family of enzymes, essential to the type II FAS pathway opens up new avenues for treating a number of infectious diseases including **malaria.**

L181 ANSWER 61 OF 71 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
ACCESSION NUMBER: 2003:36806391 BIOTECHNO
TITLE: Targeting tuberculosis and malaria through inhibition of enoyl reductase. Compound activity and structural data
AUTHOR: Kuo M.R.; Morbidoni H.R.; Alland D.; Sneddon S.F.; Gourlie B.B.; Staveski M.M.; Leonard M.; Gregory J.S.; Janjigian A.D.; Yee C.; Musser J.M.; Kreiswirth B.; Iwamoto H.; Perozzo R.; Jacobs Jr. W.R.; Sacchettini

J.C.; Fidock D.A.
CORPORATE SOURCE: J.C. Sacchettini, Dept. of Biochem. and Biophysics, Texas A and M University, Biochemistry and Biophysics Bldg., College Station, TX 77843, United States. E-mail: sacchett@tamu.edu
SOURCE: Journal of Biological Chemistry, (06 JUN 2003), 278/23 (20851-20859), 46 reference(s) CODEN: JBCHA3 ISSN: 0021-9258
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 2003:36806391 BIOTECHNO
AB Tuberculosis and **malaria** together result in an estimated 5 million deaths annually. The spread of multidrug resistance in the most pathogenic causative agents, Mycobacterium tuberculosis and Plasmodium falciparum, underscores the need to identify active compounds with novel inhibitory properties. Although genetically unrelated, both organisms use a type II fatty-acid synthase system. Enoyl acyl carrier protein reductase (ENR), a key type II enzyme, has been repeatedly validated as an effective antimicrobial target. Using high throughput inhibitor screens with a combinatorial library, we have identified two novel classes of compounds with activity against the M. tuberculosis and P. falciparum enzyme (referred to as InhA and PfENR, respectively). The crystal structure of InhA complexed with NAD.sup.+ and one of the inhibitors was determined to elucidate the mode of binding. Structural analysis of InhA with the broad spectrum antimicrobial **triclosan** revealed a unique stoichiometry where the enzyme contained either a single **triclosan** molecule, in a configuration typical of other bacterial ENR:**triclosan** structures, or harbored two **triclosan** molecules bound to the active site. Significantly, these compounds do not require activation and are effective against wild-type and drug-resistant strains of M. tuberculosis and P. falciparum. Moreover, they provide broader chemical diversity and elucidate key elements of inhibitor binding to InhA for subsequent chemical optimization.

L181 ANSWER 62 OF 71 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
ACCESSION NUMBER: 2003:37493150 BIOTECHNO
TITLE: Genome sequencing and comparative genomics of tropical disease pathogens
AUTHOR: Carlton J.M.
CORPORATE SOURCE: J.M. Carlton, The Institute for Genomic Research, 9712 Medical Center Drive, Rockville, MD 20850, United States. E-mail: carlton@tigr.org
SOURCE: Cellular Microbiology, (2003), 5/12 (861-873), 85 reference(s) CODEN: CEMIF5 ISSN: 1462-5814
DOCUMENT TYPE: Journal; General Review
COUNTRY: United Kingdom
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 2003:37493150 BIOTECHNO
AB The sequencing of eukaryotic genomes has lagged behind sequencing of organisms in the other domains of life, archae and bacteria, primarily due to their greater size and complexity. With recent advances in high-throughput technologies such as robotics and improved computational resources, the number of eukaryotic genome sequencing projects has increased significantly. Among these are a number of sequencing projects

of tropical pathogens of medical and veterinary importance, many of which are responsible for causing widespread morbidity and mortality in peoples of developing countries. Uncovering the complete gene complement of these organisms is proving to be of immense value in the development of novel methods of parasite control, such as antiparasitic drugs and vaccines, as well as the development of new diagnostic tools. Combining pathogen genome sequences with the host and vector genome sequences is promising to be a robust method for the identification of host-pathogen interactions. Finally, comparative sequencing of related species, especially of organisms used as model systems in the study of the disease, is beginning to realize its potential in the identification of genes, and the evolutionary forces that shape the genes, that are involved in evasion of the host immune response.

L181 ANSWER 63 OF 71 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
ACCESSION NUMBER: 2003:36570482 BIOTECHNO
TITLE: Lipid metabolism in Plasmodium falciparum-infected erythrocytes: Possible new targets for malaria chemotherapy
AUTHOR: Mitamura T.; Palacpac N.M.Q.
CORPORATE SOURCE: T. Mitamura, Department of Molecular Protozoology, Res. Inst. for Microbial Diseases, Osaka University, 3-1 Yamadaoka, Suita, Osaka 565-0871, Japan. E-mail: mitamura@biken.osaka-u.ac.jp
SOURCE: Microbes and Infection, (2003), 5/6 (545-552), 46 reference(s) CODEN: MCINFS ISSN: 1286-4579
DOCUMENT TYPE: Journal; General Review
COUNTRY: France
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 2003:36570482 BIOTECHNO
AB The emergence and spread of drug-resistant parasites coupled with the absence of an effective vaccine makes malaria treatment more complicated, and thus the development of new antimalarial drugs is one of the urgent tasks in malaria research. This review highlights lipid metabolism in Plasmodium parasite cells, the study of which would lead to providing new targets for therapeutic intervention. .COPYRGT. 2003 Editions scientifiques et medicales Elsevier SAS. All rights reserved.

L181 ANSWER 64 OF 71 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
ACCESSION NUMBER: 2003:36930019 BIOTECHNO
TITLE: Malaria parasite and vector genomes: Partners in crime
AUTHOR: Craig A.; Kyes S.; Ranson H.; Hemingway J.
CORPORATE SOURCE: A. Craig, Liverpool Sch. of Tropical Medicine, Pembroke Place, Liverpool L3 5QA, United Kingdom. E-mail: agcraig@liv.ac.uk
SOURCE: Trends in Parasitology, (01 AUG 2003), 19/8 (356-362), 49 reference(s) CODEN: TPRACT ISSN: 1471-4922
DOCUMENT TYPE: Journal; General Review
COUNTRY: United Kingdom
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 2003:36930019 BIOTECHNO
AB The publication of the genome sequences of the malaria parasite Plasmodium falciparum and the insect vector Anopheles gambiae paves the way for scientists to study these organisms by using technologies developed to observe global changes in transcription and translation, as well as computational tools. Researchers are now able to investigate

complex changes involved in development, growth and reaction to external factors. Given the medical importance of these organisms, much of this work is targeted on drug or insecticide discovery (including mechanisms of resistance to existing treatments), but the genome information also provides the opportunity to develop novel therapies.

L181 ANSWER 65 OF 71 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
ACCESSION NUMBER: 2003:36070378 BIOTECHNO
TITLE: A type II pathway for fatty acid biosynthesis presents drug targets in Plasmodium falciparum
AUTHOR: Waller R.F.; Ralph S.A.; Reed M.B.; Su V.; Douglas J.D.; Minnikin D.E.; Cowman A.F.; Besra G.S.; McFadden G.I.
CORPORATE SOURCE: R.F. Waller, Sch. of Biochem./Molecular Biology, University of Melbourne, Melbourne, Vic. 3010, Australia.
E-mail: rossfw@unimelb.edu.au
SOURCE: Antimicrobial Agents and Chemotherapy, (01 JAN 2003), 47/1 (297-301), 45 reference(s)
CODEN: AMACCQ ISSN: 0066-4804
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 2003:36070378 BIOTECHNO
AB It has long been held that the **malaria** parasite, Plasmodium sp., is incapable of de novo fatty acid synthesis. This view has recently been overturned with the emergence of data for the presence of a fatty acid biosynthetic pathway in the relict plastid of P. falciparum (known as the apicoplast). This pathway represents the type II pathway common to plant chloroplasts and bacteria but distinct from the type I pathway of animals including humans. Specific inhibitors of the type II pathway, thiolactomycin and **triclosan**, have been reported to target this Plasmodium pathway. Here we report further inhibitors of the plastid-based pathway that inhibit Plasmodium parasites. These include several analogues of thiolactomycin, two with sixfold-greater efficacy than thiolactomycin. We also report that parasites respond very rapidly to such inhibitors and that the greatest sensitivity is seen in ring-stage parasites. This study substantiates the importance of fatty acid synthesis for blood-stage parasite survival and shows that this pathway provides scope for the development of novel **antimalarial** drugs.

L181 ANSWER 66 OF 71 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
ACCESSION NUMBER: 2002:34952681 BIOTECHNO
TITLE: Structural elucidation of the specificity of the antibacterial agent **triclosan** for **malarial** enoyl acyl carrier protein reductase
AUTHOR: Perozzo R.; Kuo M.; Sidhu A.B.S.; Valiyaveettil J.T.; Bittman R.; Jacobs Jr. W.R.; Fidock D.A.; Sacchettini J.C.
CORPORATE SOURCE: J.C. Sacchettini, Department of Biochemistry, Texas A and M University, College Station, TX 77843-2128, United States.
E-mail: sacchett@tamu.edu
SOURCE: Journal of Biological Chemistry, (12 APR 2002), 277/15 (13106-13114), 62 reference(s)
CODEN: JBCHA3 ISSN: 0021-9258
DOCUMENT TYPE: Journal; Article
COUNTRY: United States

LANGUAGE: English
SUMMARY LANGUAGE: English
AN 2002:34952681 BIOTECHNO
AB The human **malaria** parasite Plasmodium falciparum synthesizes fatty acids using a type II pathway that is absent in humans. The final step in fatty acid elongation is catalyzed by enoyl acyl carrier protein reductase, a validated antimicrobial drug target. Here, we report the cloning and expression of the P. falciparum enoyl acyl carrier protein reductase gene, which encodes a 50-kDa protein (PfENR) predicted to target to the unique parasite apicoplast. Purified PfENR was crystallized, and its structure resolved as a binary complex with NADH, a ternary complex with **triclosan** and NAD.sup.+, and as ternary complexes bound to the **triclosan** analogs 1 and 2 with NADH. Novel structural features were identified in the PfENR binding loop region that most closely resembled bacterial homologs; elsewhere the protein was similar to ENR from the plant Brassica napus (root mean square for Cαs, 0.30 Å). **Triclosan** and its analogs 1 and 2 killed multidrug-resistant strains of intra-erythrocytic P. falciparum parasites at sub to low micromolar concentrations in vitro. These data define the structural basis of **triclosan** binding to PfENR and will facilitate structure-based optimization of PfENR inhibitors.

L181 ANSWER 67 OF 71 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
ACCESSION NUMBER: 2002:35148109 BIOTECHNO
TITLE: Genome sequence and comparative analysis of the model rodent malaria parasite Plasmodium yoelii yoelii
AUTHOR: Carlton J.M.; Angiuoli S.V.; Suh B.B.; Kooij T.W.; Pertea M.; Silva J.C.; Ermolaeva M.D.; Allen J.E.; Selengut J.D.; Koo H.L.; Peterson J.D.; Pop M.; Kosack D.S.; Shumway M.F.; Bidwell S.L.; Shallom S.J.; Van Aken S.E.; Riedmuller S.B.; Feldblyum T.V.; Cho J.K.; Quackenbush J.; Sedegah M.; Shoaibi A.; Cummings L.M.; Florens L.; Yates J.R.; Raine J.D.; Sinden R.E.; Harris M.A.; Cunningham D.A.; Preiser P.R.; Bergman L.W.; Vaidya A.B.; Van Lin L.H.; Janse C.J.; Waters A.P.; Smith H.O.; White O.R.; Salzberg S.L.; Venter J.C.; Fraser C.M.; Hoffman S.L.; Gardner M.J.; Carucci D.J.
CORPORATE SOURCE: J.M. Carlton, Institute for Genomic Research, 9712 Medical Center Drive, Rockville, MD 20850, United States.
E-mail: carlton@tigr.org
SOURCE: Nature, (03 OCT 2002), 419/6906 (512-519), 62 reference(s)
CODEN: NATUAS ISSN: 0028-0836
DOCUMENT TYPE: Journal; Article
COUNTRY: United Kingdom
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 2002:35148109 BIOTECHNO
AB Species of malaria parasite that infect rodents have long been used as models for malaria disease research. Here we report the whole-genome shotgun sequence of one species, Plasmodium yoelii yoelii, and comparative studies with the genome of the human malaria parasite Plasmodium falciparum clone 3D7. A synteny map of 2,212 P. y. yoelii contiguous DNA sequences (contigs) aligned to 14 P. falciparum chromosomes reveals marked conservation of gene synteny within the body of each chromosome. Of about 5,300 P. falciparum genes, more than 3,300 P. y. yoelii orthologues of predominantly metabolic function were

identified. Over 800 copies of a variant antigen gene located in subtelomeric regions were found. This is the first genome sequence of a model eukaryotic parasite, and it provides insight into the use of such systems in the modelling of Plasmodium biology and disease.

L181 ANSWER 68 OF 71 DRUGU COPYRIGHT 2004 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-17811 DRUGU M T S
TITLE: Antimalarial chemotherapy: young guns or back to the future
AUTHOR: Biagini G A; O'Neill P M; Nzila A; Ward S A; Bray P G
CORPORATE SOURCE: Sch.Trop.Med.Liverpool; Univ.Liverpool; Wellcome
LOCATION: Liverpool, U.K.; Nairobi, Kenya
SOURCE: Trends Parasitol. (19, No. 11, 479-87, 2003) 4 Fig. 1 Tab. 74 Ref.
ISSN: 1471-4922
AVAIL. OF DOC.: Division of Molecular and Biochemical Parasitology, Liverpool School of Tropical Medicine, Pembroke Place, Liverpool, L3 5QA, England. (P.G.B.). (e-mail: p.g.bray@liv.ac.uk).
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AN 2004-17811 DRUGU M T S
AB New advances in **antimalarial** chemotherapy are reviewed. 4-Aminoquinolines, artemisinins, antifolates, and progress in the development of newer drugs targeting membrane biosynthesis, the plasmid organelle, the cell cycle, transporters, isoprenoid biosynthesis and mitochondrial function are discussed.
ABEX Approaches to overcoming the problem of resistance in **malaria** include the novel use of older drugs, the re-design of existing drugs, and the validation of novel parasite-specific drug targets. The mode of action and mechanism of resistance to established **antimalarials** are discussed with reference to animal and clinical studies. Structure-activity relationships among 4-aminoquinolines including amodiaquine, quinine, mefloquine, chloroquine analogs, e.g. WR-268668 and pyronaridine, artemisinins such as artemether and arteether, C-10 carba and aryl analogs, e.g. TDR-40292, the peroxide analog fenozan B0-7, the endoperoxide analog arteflene, tetraoxane, and trioxaquines, the antifolates proguanil, pyrimethamine, chlorproguanil + dapsone, WR-99201 and its precursor PS-15, precursors of methotrexate and aminopterin, and pteridine analogs are described. New targets for **antimalarials** including membrane biosynthesis (choline analog G-25), the plasmid organelle (thiolactomycin, **triclosan** and allophenylnorstatin), the cell cycle (cyclin-dependent kinase inhibitors, e.g. paullones and oxindoles), transporters (dinucleoside phosphate dimers), isoprenoid biosynthesis (fosmidomycin and FR-900098) and mitochondrial function (atovaquone and proguanil). (E33/JB)

L181 ANSWER 69 OF 71 DRUGU COPYRIGHT 2004 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-11279 DRUGU M T S
TITLE: **Triclosan**: a shot in the arm for **antimalarial** chemotherapy.
AUTHOR: Rao S P R; Surolia A; Surolia N
CORPORATE SOURCE: Indian-Inst.Sci.Bangalore; Jawaharlal-Nehru-Cent.Adv.Sci.Res.
LOCATION: Bangalore, India
SOURCE: Mol.Cell.Biochem. (253, No. 1-2, 55-63, 2003) 3 Fig. 1 Tab. 98 Ref.
CODEN: MCBIB8 ISSN: 0300-8177
AVAIL. OF DOC.: Molecular Biophysics Unit, Indian Institute of Science, Bangalore 560012, India. (A.S.). (e-mail: surolia@mbu.iisc.ernet.in).
LANGUAGE: English

DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AN 2004-11279 DRUGU M T S
AB **Triclosan** as therapy for **malaria** was reviewed, with reference to its mode of action, application, safety and toxicity. The recently discovered plasmodial fatty acid biosynthetic pathway and its inhibition by **triclosan** could be a crucial breakthrough in the fight against **malaria.** **Triclosan** is well tolerated, proven by its usage for decades in human consumer goods. It is used in oral health, as an antibacterial agent. **Triclosan** has little toxicity in studies in rats and monkeys. **Triclosan** promises to be far superior to any other single **antimalarial** agent. (No EX).
ABEX (SB)

L181 ANSWER 70 OF 71 DRUGU COPYRIGHT 2004 THE THOMSON CORP on STN
ACCESSION NUMBER: 2003-03403 DRUGU M T
TITLE: New therapeutic strategies in the treatment of malaria.
AUTHOR: Kaiser A; Maier W
CORPORATE SOURCE: Inst.Med.Parasitol.Bonn
LOCATION: Bonn, Ger.
SOURCE: Dtsch.Med.Wochenschr. (127, No. 30, 1595-1600, 2002) 3 Fig. 2 Tab. 30 Ref.
CODEN: DMWOAX ISSN: 0012-0472
AVAIL. OF DOC.: Institut fuer Medizinische Parasitolgie, Bonn, Germany. (e-mail: akaiser@parasit.meb.uni- bonn.de).
LANGUAGE: German
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AN 2003-03403 DRUGU M T
AB Modern aspects of **malaria** therapy are reviewed with reference to molecular targeting of parasite-specific genes including those involved in isoprenoid biogenesis, inhibition of fatty acid biosynthesis and polyamine biosynthesis as a possible target for chemotherapy against Plasmodium falciparum. Indications for therapy with 4-aminoquinolines, 8-aminoquinolines and phenanthrenes are discussed. Chemotherapeutic drug combinations currently being evaluated in phase 1/3 clinical studies include chloroproguanil/dapsone/artesunate and artesunate/mefloquine.
ABEX Increasing levels of resistance in modern strains of P. falciparum and P. vivax have led to conventional **antimalarial** drugs such as chloroquine and fixed combinations of pyrimethamine + sulfadoxine becoming less reliable. This has led to a search for new chemotherapeutics targeted at specific metabolic aspects of the **malarial** parasites. The range of drugs currently available includes 4-aminoquinolines (quinine, chloroquine, amodiaquine, mefloquine), 8-aminoquinolines (primaquine), phenanthrenes (halofantrine), pyrimethamine, proguanil, atovaquone and atovaquone + proguanil. New drug combinations currently undergoing clinical evaluation include choloroproguanil + dapsone + artesunate (targeted against fatty acid biosynthesis) and artesunate + mefloquine (targeted against isoprenoid biosynthesis). The isoprenoid biosynthetic pathway of P. falciparum represents a parasite-specific target for **antimalarial** drugs, and the enzyme 1-deoxy-D-xylulose reductase can be inhibited by drugs including fosmidomycin. The fatty acid biosynthetic pathway in P. falciparum is another drug target and the disinfectant/antiseptic agent, **triclosan** (5-chloro-2-(2,4-dichlorophenoxy)phenol), has been shown to inhibit enoyl-ACP-reductase in **malarial** parasites. Genes of polyamine (putrescine, spermidine,

spermine) biosynthesis represent a third target for new **antimalarial** drugs, and D,D-alpha-difluoromethylornithine (eflornithine) inhibit ornithine decarboxylase in in-vitro cultures of P. falciparum. The enzymes deoxyhypusine synthase and homospermidine synthase are also potential targets for **antimalarial** drugs. (S67/FM) Neue Therapieansaetze zur Behandlung der **Malaria.**

L181 ANSWER 71 OF 71 DRUGU COPYRIGHT 2004 THE THOMSON CORP on STN
ACCESSION NUMBER: 1995-41017 DRUGU M B
TITLE: The mode of action of 8-aminoquinoline in Leishmania.
AUTHOR: Liu H; Nolan L L
CORPORATE SOURCE: Univ.Massachusetts
LOCATION: Amherst, Mass., USA
SOURCE: Abstr.Gen.Meet.Am.Soc.Microbiol. (95, Meet., 152, 1995)
ISSN: 0067-2777
AVAIL. OF DOC.: School of Public Health and Health Science, University of Massachusetts, Amherst, MA, U.S.A.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AN 1995-41017 DRUGU M B
AB 8-Aminoquinoline compounds (developed as **antimalarials**) were tested for inhibitory activity against Leishmania mexicana to determine their inhibitory properties. In particular, WR-242511 inhibited the growth of leishmanial cells as a result of inhibiting (in turn) DNA, RNA, fatty acid and then protein synthesis. Further studies suggested that WR-242511 interferes with the catenation and decatenation of the mitochondria kinetoplast DNA (kDNA) network through inhibition of the type II topoisomerase. Subsequently inhibition of DNA synthesis leads to the death of the leishmanial cells. (conference abstract).
ABEX The **antimalarial** 8-aminoquinoline, WR-242511, demonstrated strong inhibition to the growth of leishmanial cells in-vitro. Its IC50 was 2.5 uM against L. mexicana 227. The mode of action of WR-242511 on DNA, RNA, protein and fatty acid synthesis of leishmanial cells was investigated utilizing radioactive substrates. The results suggested that it inhibits DNA synthesis initially, RNA synthesis then declines.Protein synthesis is the last metabolic pathway to be affected. This is possibly due to the **inhibition** of DNA and RNA **synthesis.** The **inhibition** of **fatty acid synthesis** was observed after the **inhibition** of RNA **synthesis** and 2 hr after exposure to WR-242511. The Authors also investigated the effect of WR-242511 on the kinetoplast DNA of leishmanial cells. Type II topoisomerase controls the catenation and supercoiling of minicircle DNA of the kDNA network in mitochondria. The effect of WR-242511 on type II topoisomerase in mitochondria of L. mexicana 227 was studied by detecting the amount of free minicircle DNA in the drug-treated cells. The results demonstrated that the free minicircle DNA increased WR-242511-treated leishmanial cells. (E54/RSV)

=> => d que nos l183
L23 44 SEA FILE=REGISTRY ABB=ON PLU=ON 3380-34-5/RN,CRN
L24 1 SEA FILE=REGISTRY ABB=ON PLU=ON 17397-89-6/RN,CRN
L39 SCR 2043 2052 2050
L40 SCR 1929
L42 STR
L44 4711 SEA FILE=REGISTRY SSS FUL ((L40 NOT L39) AND L42)
L46 STR

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L52             STR
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L55          48 SEA FILE=REGISTRY ABB=ON  PLU=ON  L23 OR L24 OR L54
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                GENUS)"+PFT,NT/CT
L62        1804 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "PLASMODIUM BERGHEI"+PFT,NT/CT

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L67           8 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "FATTY ACID?"/CW
L68        2534 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L55
L69          42 SEA FILE=HCAPLUS ABB=ON  PLU=ON  3380-34-5D?
L70         421 SEA FILE=HCAPLUS ABB=ON  PLU=ON  17397-89-6?
L71         417 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ((L59 OR L60 OR L61 OR L62 OR
                L63)) AND ((L64 OR L65 OR L66 OR L67))
L72          28 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L59 OR L60 OR L61 OR L62 OR
                L63) AND (L68 OR L69 OR L70)
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L77       22131 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L64 OR L65 OR L66 OR L67)
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L80        3768 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L75 (L) L77
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L82          43 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L72 OR L81
L182          7 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L54
L183          7 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L182 NOT L82


=> d ibib abs ed hitstr l183
YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS' - CONTINUE? (Y)/N:y


L183 ANSWER 1 OF 7  HCAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:         1984:451309  HCAPLUS
DOCUMENT NUMBER:          101:51309
TITLE:                    Unsymmetrical fluorescein derivatives
INVENTOR(S):              Khanna, Pyare; Colvin, Warren
PATENT ASSIGNEE(S):       Syva Co., USA
SOURCE:                   U.S., 14 pp.
                          CODEN: USXXAM
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
     ---------------      ----   --------    --------------------     --------
     US 4439356            A     19840327    US 1981-240031           19810303
     US 4652531            A     19870324    US 1984-587085           19840307
PRIORITY APPLN. INFO.:                       US 1981-240031      A3   19810303
```

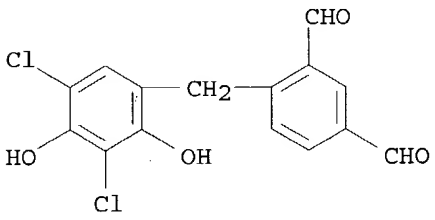
AB Unsym. fluorescein derivs. were prepared, particularly 1,8-unsubstituted-9-substituted-6-hydroxy-3H-xanthen-3-ones, having 1 aliphatic substituent at any of the remaining positions, where the aliphatic substituent is separated from the annular C atom by 0-1 O atom. These fluorescent compds. have absorption maximum in 0.5M phosphate buffer pH 8 usually at least .apprx.500 nm, and they can be used to reduce background fluorescence interference occurred in chemical anal. They are potentially useful for detection or determination of proteins, polysaccharides, nucleic acids, drugs, metabolites and others by competitive protein binding assays, e.g., immunoassay.

ED Entered STN: 18 Aug 1984

IT **91000-77-0**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with resorcinol derivs.)

RN 91000-77-0 HCAPLUS

CN 1,3-Benzenedicarboxaldehyde, 4-[(3,5-dichloro-2,4-dihydroxyphenyl)methyl]- (9CI) (CA INDEX NAME)



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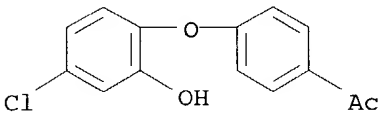
YOU HAVE REQUESTED DATA FROM 6 ANSWERS - CONTINUE? Y/(N):y

L183 ANSWER 2 OF 7 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1972:430329 HCAPLUS
DOCUMENT NUMBER: 77:30329
TITLE: Halogenated diphenyl ether-containing disinfectants
INVENTOR(S): Model, Ernst; Bindler, Jakob
PATENT ASSIGNEE(S): Geigy Chemical Corp.
SOURCE: U.S., 21 pp. Continuation of U.S. 3,506,720 (See NETH Appl. 64 01,526, CA 63;11431b).
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 3629477	A	19711221	US 1967-627603		19670403
US 3784698	A	19740108	US 1970-70190		19700908
US 3800048	A	19740326	US 1970-74896		19700923
PRIORITY APPLN. INFO.:			US 1964-345080	A2	19640217
			US 1966-570742	A2	19660808
			US 1967-627603	A3	19670403

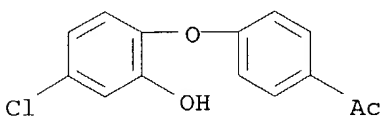
AB Various halogenated diphenyl ethers were used to control microbial growth. The compds. were incorporated into toilet soaps, textile washing prepns., cleansers, mouthwashes, prepns. for treating urinary and intestinal infections, and agricultural wettable powders, granules, pastes, and emulsions. 4,4'-Dichloro-2-hydroxydiphenyl ether (I) [3380-30-1] and 4,2',4'-trichloro-2-hydroxydiphenyl ether (II) [3380-34-5] inhibited the germination of Alternaria tenuis and Botrytis cinerea, and the growth of Bacillus, Sarcina, Streptococcus, Salmonella, Staphylococcus, Proteus, Brevibacterium, and Escherichia species.
ED Entered STN: 12 May 1984
IT **3380-52-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 3380-52-7 HCAPLUS
CN Ethanone, 1-[4-(4-chloro-2-hydroxyphenoxy)phenyl]- (9CI) (CA INDEX NAME)



L183 ANSWER 3 OF 7 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1969:56699 HCAPLUS
DOCUMENT NUMBER: 70:56699
TITLE: Antimicrobial substances
INVENTOR(S): Bindler, Jakob; Model, Ernst
PATENT ASSIGNEE(S): Geigy, J. R., A.-G.
SOURCE: Patentschrift (Switz.), 4 pp. Addn. to Swiss 432119
CODEN: SWXXAS
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CH 460443		19680930	CH	19640219

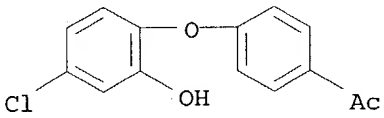
AB Compds. such as 4-chloro-4'-acetyl-2-hydroxydiphenyl ether, 4,4'-dichloro-2'-cyano-2-hydroxydiphenyl ether, 4,4'-dichloro-2'-amino-2-hydroxydiphenyl ether and 4,4'-dichloro-3-allyl-2-hydroxydiphenyl ether impregnated on textile fibers and films prevents the growth of bacteria and fungi.
ED Entered STN: 12 May 1984
IT **3380-52-7**
RL: BIOL (Biological study)
(textile fibers impregnated with, microorganism resistant)
RN 3380-52-7 HCAPLUS
CN Ethanone, 1-[4-(4-chloro-2-hydroxyphenoxy)phenyl]- (9CI) (CA INDEX NAME)



L183 ANSWER 4 OF 7 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1968:437058 HCAPLUS
DOCUMENT NUMBER: 69:37058
TITLE: Antimicrobial finishing of textiles
INVENTOR(S): Bindler, Jakob; Model, Ernst
PATENT ASSIGNEE(S): Geigy, J. R., A. -G.
SOURCE: Patentschrift (Switz.), 4 pp. Addn. to Swiss 406127
CODEN: SWXXAS
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CH 450348		19680430	CH	19640219

GI For diagram(s), see printed CA Issue.
AB Antimicrobial properties are imparted to textiles by treatment with an allyl-, NC-, H2N-, or Ac-substituted, halogenated o-hydroxydiphenyl ether, e.g. 4-chloro-4'-acetyl-2-hydroxydiphenyl ether; 4,4'-dichloro-2'-cyano-2-hydroxydiphenyl ether; 4,4'-dichloro-2'-amino-2-hydroxydiphenyl ether; or 4,4'-dichloro-3-allyl-2-hydroxydiphenyl ether (I). To a laundering solution containing 0.3 g./l. octylphenol-polyglycol ether and 1.7 g./l. Na polyphosphate, one of the above compds. was added at 25 mg./l. as a 5% solution in MeOCH2CH2OH. Cotton cambric (1 part) was washed for 20 min. at 90° in 20 parts solution, rinsed with soft H2O, centrifuged, dried, and ironed. Tests with Staphylococcus aureus and Escherichia coli showed that samples treated as above prevented growth of these bacteria.
ED Entered STN: 12 May 1984
IT **3380-52-7**
RL: USES (Uses)
(as bactericide for textiles)
RN 3380-52-7 HCAPLUS
CN Ethanone, 1-[4-(4-chloro-2-hydroxyphenoxy)phenyl]- (9CI) (CA INDEX NAME)



L183 ANSWER 5 OF 7 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1966:11264 HCAPLUS
DOCUMENT NUMBER: 64:11264
ORIGINAL REFERENCE NO.: 64:2010c-h,2011a-b
TITLE: Esters of halogenated 2-phenoxyphenols
PATENT ASSIGNEE(S): J. R. Geigy A.-G.
SOURCE: 47 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
BE 659636		19650812	BE	
FR 1441499			FR	
NL 6501783			NL	

PRIORITY APPLN. INFO.: CH 19640214
GI For diagram(s), see printed CA Issue.
AB Esters, mostly of type I, in which R is acyl and R1, R2, R3 and R4 are H, halogen or other groups, are described. Their bacteriostatic activity against gram-pos. and gram-neg. organisms, as well as their inhibition of pathogenic mycetes, make them useful in sterilizing fibers and in the treatment of urinary infections. The intermediate 2-phenoxyphenols (II) were made by various methods. Method 1. 1-(4-Chlorophenoxy)-2-nitro-4-chlorobenzene was reduced by Fe and aqueous AcOH to 1-(4-chlorophenoxy)-2-amino-4-chlorobenzene, m. 67°, from which in turn was prepared the 1-(4-chlorophenoxy)-2-hydroxy-4-chlorobenzene, b12-13 201-6°, m. 78-9° (petr. ether). Method 2. 1-(2-Chloro-4-nitrophenoxy)-2-methoxy-4-chlorobenzene, m. 159-61°, was catalytically reduced to 1-(2-chloro-4-aminophenoxy)-2-methoxy-4-chlorobenzene, m. 100-2°, which subjected to the Sandmeyer reaction yielded 1-(2,4-dichlorophenoxy)-2-methoxy-4-chlorobenzene (III), m. 210-17°. AlCl3 (243 g.) was added to a solution of 187.5 g. III in 800 ml. C6H6, the mixture refluxed for 0.5 hr., then poured on ice-HCl to give 1-(2,4-dichlorophenoxy)-2-hydroxy-4-chlorobenzene, m. 60-1°. Method 3. A solution of 1-phenoxy-2-methoxybenzene in 500 ml. AcOH was treated at 50° with 74 g. Cl to give 1-(4-chlorophenoxy)-2-methoxy-5-chlorobenzene, b0.4 144-7°, which on demethylation yielded 1-(4-chlorophenoxy)-2-hydroxy-5-chlorobenzene, m. 78-9°. Method 4. On heating 1-(4-chlorophenoxy)-2-allyloxy-4-chlorobenzene, m. 67-9°, to 230-50°, the 1-(4-chlorophenoxy)-2-hydroxy-3-allyl-4-chlorobenzene, b1, 158-64°, was obtained. Other intermediates prepared were: 1-(2-nitro-4-chlorophenoxy)-2-methoxy-4-chlorobenzene, an oil; 1-(2-amino-4-chlorophenoxy)-2-methoxy-4-chlorobenzene, m. 73-6°; 1-(2-cyano-4-chlorophenoxy)-2-methoxy-4-chlorobenzene, b0.2-0.3 185-96°; 1-(4-chlorophenoxy)-2-methoxy-4-chlorobenzene, b12 197-203°; 1-(4-acetylphenoxy)-2-methoxy-4-chlorobenzene, b0.07 172-80°. Also described were these II (R1, R2, R3, R4 and properties given): H, H, H, 4-Cl, m. 86-8°; H, H, 2-Cl, 4-Cl, b12-13 192-6°; H, 4-Cl, H, H, m. 74-5°; H, 4-Cl, H, 4-Br, m. 79-80°; H, 4-Cl, H, 4-F, m. 77-8°; H, 4-Cl, 2-Cl, H, m. 61-2°; H, 4-Cl, 3-Cl, 4-Cl, m. 103-4°; H, 4-Cl, 3-Me, 4-Cl, m. 118-19°; H, 4-Br, H, H, m. 83-5°; H, 4-Br, H, 4-Cl, b13 214-15°; H, 4-Br, H, 4-Br, m. 53-4°; H, 4-Cl, H, 4-MeO, b12 206-11°; H, 4-Cl, 3-CF3, 4-Cl, m. 63-5°; 4-Cl, 5-Me, H, 4-Cl, m. 93-4°; 4-Cl, 6-Cl, H, 4-Cl, m. 81-2°; 4-Cl, 6-Cl, 2-Cl, 4-Cl, b11 219-22°; H, 6-Cl, 2-Cl, 4-Cl, b12 200-3°; H, 6-Cl, H, 4-Cl, m. 80-1°; H, 4-Br, 2-Cl, 4-Cl, b12-13 225-9°; H, 4-Br, 2-Br, 4-Br, b0.06 170-3°; H, 4-Cl, 2-CN, 4-Cl, m. 145-6°; 4-Cl, 5-Cl, 2-Cl, 4-Cl, m. 89-90°; H, 4-Cl, H 4-I, m. 86-8°; 4-Cl, 5-Cl, H, 4-Cl, m. 96-7°; H, 4-Cl, 2-NH2, 4-Cl, m. 126-8°; H, 5-Cl, H, H, b12 174-9°; H, 4-Cl, H, 4-Ac, m. 114-15°. Also prepared were 1-(2,4,5-trichlorophenoxy)-2-hydroxybenzene, b0.05 140-5°; 1-(2,4,5-trichlorophenoxy)-2-hydroxy-4-chlorobenzene, m. 147-8°; 1-(4-chlorophenoxy)-2-hydroxy-3,5-dimethyl-4-chlorobenzene, m. 116°; 1-(2-isopropyl-4-chloro-5-methylphenoxy)-1-hydroxy-4-chlorobenzene, b10 211-16°. The esters (I) were prepared from II by conventional methods; made were these I (R, R1, R2, R3, R4 and properties given): Ac, H, 4-Cl, H, 4-Cl, b0.08 156-60°; Ac, H, 4-Cl, 2-Cl, 4-Cl, b0.05 175-7°; Ac, H, 4-Br, H, 4-Br, b0.06 168-72°; MeCH:CHCO, H, 4-Cl, H, 4-Cl, b0.15 166-8°; EtCO, H, 4-Cl, 2-Cl, 4-Cl, b0.03 162-5°; Bz, H, 4-Cl, 2-Cl, 4-Cl, b0.05 211-16°; Me2NCO, H, 4-Cl, H, 4-Cl, b0.09 194-7°; EtOCO, H, 4-Cl, 2-Cl, 4-Cl, b0.09 174-8°; Cl-CH2CO, H, 4-Cl, 2-Cl, 4-Cl, b0.1 188-94°; Me(CH2)6CO, H, 4-Cl, H, 4-Cl, b0.08 189-97°; Me(CH2)16CO, H, 4-Cl, H, 4-Cl, b0.075

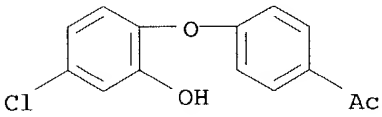
212-18°; Me(CH2)16CO, H, 4-Cl, H, 4-Cl, b0.09 246-57°; ClCH2CO, H, 4-Cl, H, 4-Cl, b0.1 162-7°; MeHNCO, 4-Cl, 5-Cl, H, 4-Cl, m. 122-4°; Bz, H, 4-Cl, H, 4-Cl, b0.015 200-5°; p-ClC6H4CO, H, 4-Cl, H, 4-Cl, b0.1 220-5°; Cl2HCCO, H, 4-Cl, 2-Cl, 4-Cl, b0.3 182-94°; Cl3CCO, H, 4-Cl, 2-Cl, 4-Cl, b0.09 189-95°; Me3CCO, H, 4-Cl, H, 4-Cl, b0.05 161-6°; Me3CCO, H, 4-Cl, 2-Cl, 4-Cl, b0.06 171-7°; MeSO2, H, 4-Cl, H, 4-Cl, m. 113.5-15°; ClCH2SO2, H, 4-Cl, H, 4-Cl, b0.1 186-91°; also prepared was the bis[2-(4-chlorophenoxy)-5-chlorophenyl] ester of fumaric acid, m. 147-8°.

ED Entered STN: 22 Apr 2001

IT **3380-52-7**, Acetophenone, 4'-(4-chloro-2-hydroxyphenoxy)- (preparation of)

RN 3380-52-7 HCAPLUS

CN Ethanone, 1-[4-(4-chloro-2-hydroxyphenoxy)phenyl]- (9CI) (CA INDEX NAME)



L183 ANSWER 6 OF 7 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1965:462728 HCAPLUS

DOCUMENT NUMBER: 63:62728

ORIGINAL REFERENCE NO.: 63:11431b-g

TITLE: Preparation of halogenated 2-hydroxydiphenyl ethers

PATENT ASSIGNEE(S): J. R. Geigy A.-G.

SOURCE: 24 pp.

DOCUMENT TYPE: Patent

LANGUAGE: Unavailable

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
NL 6401526		19640824	NL	
PRIORITY APPLN. INFO.:			CH	19630222

GI For diagram(s), see printed CA Issue.

AB I and their O-acyl derivs. are biocides and are used in the protection of organic materials against gram-pos. and gram-neg. bacteria. I are insol. in H2O, but soluble in dilute NaOH, KOH, and organic solvents; they can be used in soaps, laundry solution, incorporated in polymers and combined with other antibacterials. I are prepared by boiling the corresponding diazonium derivative of 2-aminoalkylhalodiphenyl ethers, which are obtained by condensation of the corresponding 1-nitro-2-halobenzenes with phenols or phenolates, followed by the reduction of the halogenated 2-nitrodiphenyl ether. Another method consists in the condensation of 1-nitro-2 or 4-halobenzenes with 1-hydroxy-2-alkoxybenzenes, followed by the dealkylation of the alkoxy group and reduction of the nitro group, and diazotization of the obtained amine, the diazo group can then be exchanged for H or a halogen; 1-alkoxy-2-halobenzenes can be condensed with alkali salts of halo phenols in the presence of Cu++ or Cu+ salts, followed by dealkylation; 2-hydroxydiphenyl ethers can be halogenated to give I; 2-chlorobenzoic acids can be condensed with 2-alkoxyphenols, followed by decarboxylation and dealkylation. The I prepared are tabulated: R4, R5, R3, R2, R1, R, M.p. or b.p.; H, H, Cl, H, H, Cl, b12-13, 192-6°; H, H, Cl, H, Cl, Cl, b0.06, 140-5°; Cl, H, H, H, Cl, H, m.,

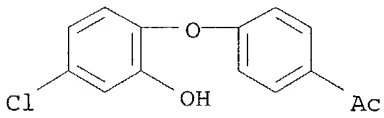
78-9°; Cl, H, H, H, Br, H, m., 79-80°; Cl, H, H, H, F, H, m., 77-8°; Cl, H, H, Cl, Cl, H, m.,103-4°; Cl, H, Cl, H, Cl, H, m., 60-1°; Cl, H, Cl, H, Cl, Cl, m., 147-8°; Cl, H, H, Me, Cl, H, m., 118-19°; Br, H, H, H, Cl, H, b13, 214-15°; Br, H, H, H, H, H, m., 83-5°; Br, H, H, H, Br, H, m., 53-4°; Cl, H, H, H, OMe, H, b13, 206-7°; Cl, H, H, CF3, Cl, H, m., 63-5°; Cl, H, H, H, H, H, m., 74-5°; Cl, H, H, H, I, H, m., 86-8°; Cl, H, Cl, H, H, H, m., 61-2°; Cl, Cl, Cl, H, Cl, H, m., 89-90°; Br, H, Cl, H, Cl, H, b13, 215-29°; H, H, H, H, Cl, H, m., 86-8°; Cl, H, CN, H, Cl, H, m., 145-6°;Cl, H, NH2, H, Cl, H, m., 126-8°; H, H, H, Cl, Cl, H, b13, 198-200°; Cl, Cl, H, H, Cl, H, m., 96-7°; H, Cl, H, H, Cl, H, m., 78-9°; H, H, H, H, H, H, m., 78-9°; H, Cl, H, H, OAc, H, m., 114-115° The following O-acyl deriv, of I (R3 = R2 = R = H): Acyl, R4, R5, R1, B.p. or m.p.; Ac, Cl, H, Cl, b0.08, 156-60°; ClCH2CO, Cl, H, Cl, b0.1, 162-7°; MeNH.CO, Cl, Cl, Cl, m., 122-4°; Bz, Cl, H, Cl, b0.016, 200-5°; p-ClC6H4CO, Cl, H, Cl, m., 113.5-15.0°; MeSO, Cl, H, Cl, b0.1, 186-9° I have been tested in various applications against Staphylococcus aureus SG 511 and Escherichia coli 96; at concentration of 1-200 ppm., complete inhibition is obtained.

ED Entered STN: 22 Apr 2001

IT **3380-52-7**, Acetophenone, 4'-(4-chloro-2-hydroxyphenoxy)- (preparation of)

RN 3380-52-7 HCAPLUS

CN Ethanone, 1-[4-(4-chloro-2-hydroxyphenoxy)phenyl]- (9CI) (CA INDEX NAME)



L183 ANSWER 7 OF 7 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1958:20993 HCAPLUS

DOCUMENT NUMBER: 52:20993

ORIGINAL REFERENCE NO.: 52:3744c-i,3745a-i,3746a

TITLE: Complex forming tetracycline-like compounds

AUTHOR(S): Moshfegh, A.; Fallab, S.; Erlenmeyer, H.

CORPORATE SOURCE: Univ. of Basel, Switz.

SOURCE: Helvetica Chimica Acta (1957), 40, 1157-66
CODEN: HCACAV; ISSN: 0018-019X

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

AB cf. C.A. 47, 12624f. In consideration of the dependence of the activity of the tetracyclines on their ability to form metal-ion complexes, several benzophenone and diphenylmethane derivs., structural analogs of terramycin, were prepared by the Baeyer, Friedel-Crafts, and Fries reactions. Concentrated H2SO4 (120 cc.) stirred below 0° with 30 g. p-ClC6H4OH in 70 cc. MeOH and 7 cc. H2O at -10° and the mixt, treated dropwise in 2 hrs. with 9.0 g. 38% HCHO, stirred 2 hrs. at -5 to 0°, poured onto 700 g. ice, filtered, and the H2O-washed precipitate dried at 12 mm. over CaCl2 gave 29-31 g. [5,2-Cl(HO)C6H3]2CH2 (I), m. 176-7° (after sublimation at 144-50°/0.04 mm.), giving a green-brown color with FeCl3. I (10 g.) and 3 g. NaOH in 40 cc. H2O stirred 30 min. with dropwise addition of 11.6 g. Me2SO4 with cooling, refluxed 2 hrs. at 70-80°, the cooled solution extracted with 200 cc. Et2O, the dried extract evaporated, and the residue stored and filtered gave 11

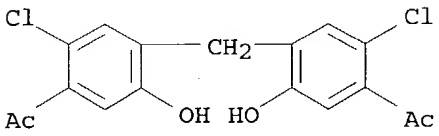
g. [5,2-Cl(EtO)C6H3]2CH2 (II), m. 122-4° (C6H6 or petr. ether), also obtained by condensation of p-ClC6H4OEt with HCHO in the presence of H2SO4. II (3.5 g.) in 30 cc. AcOH warmed briefly on a steam bath with 4.58 g. CrO3 in 5 cc. H2O, the green solution gently refluxed 14 hrs., cooled, diluted with 100 cc. H2O, filtered, and the residue washed with 30% AcOH and H2O gave 2.7 g. [5,2-Cl(EtO)C6H3]2CO (III), m. 99-102° (petr. ether). AlCl3 (30 g.) and 6 g. III refluxed 16 hrs. in 120 cc. CS2, decanted, the residue (decomposed by stirring with 100 cc. concentrated HCl and 200 g. ice, filtered, the filter cake washed with H2O, the dried product (4.5 g.) crystallized from petr. ether, and the yellow leaflets, m. 152-5°, purified through the Na salt with C give yellow needles of [5,2-Cl(HO)C6H3]2CO (IV), m. 152-5°, giving a brown-red FeCl3 reaction, and converted by refluxing with Ac2O in the presence of a trace of concentrated H2SO4 to the corresponding 2,2'-(AcO)2 compound (IVa), m. 98° (petr. ether). Finely powdered anhydrous AlCl3 (2 g.) heated to 120-40°, stirred with 1 g. IVa, the mixture heated 30 min. at 170-80°, the cooled melt decomposed by stirring with 20 cc. concentrated HCl and 40 g. ice, stored 2 hrs., filtered, the filter cake washed with hot H2O, and the product (8.8 g.) sublimed at 180-90°/0.01 mm. gave prisms of [5,3,2-Cl(AcO)(HO)C6H2)2CO (V), m. 222-4°, giving a brown-red reaction with FeCl3. V (1 g.) in 200 cc. N NaOH treated with 4 g. iodine and 8 g. KI in 30 cc. H2O, the mixture warmed 30 min. at 70°, kept 14 hrs. at 20°, filtered, the filtrate treated with 1 g. NaHSO3, acidified with 2N H2SO4, the precipitated acid taken up in 100 cc. Et2O, the solution extracted with 10% NaHCO3, and the extract acidified with 2N H2SO4 and filtered gave 0.9 g. material, sublimed at 260-5°/0.01 mm. to yellow prisms of [5,2,3-Cl(HO)(HO2C)C6H2]2CO (VI), m. 295-7°, giving a wine-red FeCl3 reaction. On account of their structure both V and VI can be regarded as terramycinlike complex-forming compds. AlCl3 (2 g.) stirred at 120-30° with 1.5 g. I diacetate 30 min. at 170-80° in the absence of moisture, the green mass stirred 1-2 hrs. with 20 cc. concentrated HCl and 50 g. ice, filtered, the filter cake washed with H2O and MeOH, crystallized from Me2CO or Et2O, and the crystals (1.35 g.) sublimed at 155-60°/0.01 mm. gave [5,3,2-ClAc(HO)C6H2]2CH2 (VII), m. 202-3°, giving a brown-violet FeCl3 reaction. The sublimation residue crystallized from Me2CO yielded a small amount of di-Ac isomer of VII, m. 220-3°, with no FeCl3 reaction. AlCl3 (64 g.) stirred at 150-60° with 32 g. p-ClC6H4OAc, the mixture heated 20 min., poured into 500 g. ice with stirring, filtered, and the washed and dried product (31.5 g.) crystallized from dilute MeOH gave 4,2-ClAcC6H3OH, m. 54°. The phenol (5 g.) in 50 cc. concentrated H2SO4 and 25 cc. MeOH stirred with dropwise addition of 2 cc. 38% HCHO with cooling, the mixture stirred 1-5 hrs. at 20° and 4 hrs. at 60-70°, stored 12 hrs., stirred with 300 cc. H2O, filtered, and the washed precipitate dried at 70° gave 5.15 g. product, m. 195-200°, sublimed at 175-85°/0.01 mm. to 70% pure VII. VII (1 g.) in 200 cc. N NaOH shaken with 4 g. iodine and 8 g. KI in 30 cc. H2O, heated 30 min. on a steam bath, stored 14 hrs., filtered, the filtrate treated with 0.5-1.0 g. NaHSO3, acidified with 2N H2SO4, filtered, the precipitate taken up in 100 cc. Et2O, the solution extracted with 10% NaHCO3, and the extract acidified yielded [5,2,3-Cl(HO)(HO2C)C6H2]2CH2 (VIII), m. 280-4° (after sublimation at 230-5°/0.01 mm.), giving a blue-violet FeCl3 reaction. Attempts to carry out the above syntheses by the Friedel-Crafts procedure gave several interesting results. AlCl3 (11 g.) and 30 g. MeOPh in 60 cc. dry CS2 at 5-10° stirred with dropwise addition of 15 g.

3,2-Me(AcO)C6H3COCl (IX) in 50 cc. CS2 with cooling to 10-15°, the mixture stirred 8 hrs. at 20°, decomposed with 100 g. ice and 50 cc. concentrated HCl, the product extracted with Et2O, the extract washed with saturated NaHCO3 solution, dried, evaporated, and the residue crystallized from alc. gave 5.6 g. x-[3,2-Me(AcO)C6H3CO]C6H4OMe (X), m. 100-1°. Similarly, condensation of IX with 1,4-(MeO)2C6H4 gave 2-acetoxy-2',5'-dimethoxy-3-methylbenzophenone (Xa), m. 139° (alc.). Xa (0.3 g.) refluxed 8 hrs. with 20 cc. 2N NaOH, the clear solution extracted twice with 500 cc. Et2O, and the aqueous solution acidified with 2N HCl gave 0.14 g. 3,2-Me(HO)C6H3CO2H (XI), m. 164°. Evaporation of the Et2O extract gave 0.12 g. p-(MeO)2C6H4. Xa (0.5 g.) in 20 cc. MeOH refluxed 16 hrs. with 0.04 g. Na in 0.031 cc. H2O and 10 cc. MeOH, the MeOH evaporated, and the residue taken up in 20 cc. H2O and filtered, the residue extracted with Et2O to give 0.2 g. p-(MeO)2C6H4, and the filtrate acidified with '2N HCl yielded 0.25 g. XI. XI (35 g.) and 300 g. KOH vigorously stirred at 210-20° in 55 cc. H2O, treated portionwise during 1.5 hrs. with 180-200 g. PbO2, stirred 20 min., the oil bath removed, the yellow-orange melt diluted slowly with stirring with 500 cc. H2O, filtered, the residue washed with warm H2O, the filtrate and washings carefully adjusted with 1:2 dilute H2SO4 to pH 9-10, filtered, and the filtrate acidified to litmus and cooled gave 35.5 g. 2-hydroxyisophthalic acid (XII), m. 237-40°; di-Me ester, m. 70-2°. The ester (14.5 g.) in 130 cc. boiling MeOH treated with 1.6 g. Na in 30 cc. MeOH and 1.24 cc. H2O gave the Na salt, m. above 360°, converted by solution in hot H2O and acidification of the cooled solution with 2N H2SO4 to the H Me 2-hydroxyisophthalate (XIIa), m. 132-5°, transformed with PCl5 to the corresponding acid chloride (XIIb). Finely powdered AlCl3 stirred at 0-5° treated dropwise with 200 cc. absolute CS2, 15 cc. p-MeC6H4OMe, and finally, within 2 hrs., with 10 g. XIIb, the mixture stirred 8 hrs., kept 14 hrs. at 20°, decanted, the residue diluted with C6H6, again decanted, the residue warmed in vacuo, stirred with 50 cc. concentrated HCl and 150 g. ice, the mixture extracted with 200 cc. C6H6, the extract washed with aqueous NaHCO3, evaporated, the yellow residue (6.2 g.) boiled 2 hrs. with 2N HCl, cooled, filtered, the crystalline residue sublimed at 151-3°/0.02 mm., and the sublimate recrystd. from Me2CO-petr. ether gave 0.2 g. 2,3-HO[5,2-Me(MeO)C6H3CO]C6H3CO2H (XIII), m. 166-7°, giving a red-violet FeCl3 reaction. The aqueous NaHCO3 washings on acidification yielded a mixture of the acids XII, XIIa, and XIII, which, boiled in 100 cc. H2O, filtered hot, the residue boiled with 30 cc. H2O, filtered, and the H2O-insol. residue (0.3 g.) sublimed at 151-3°/0.02 mm. gave 0.2 g. XIII. Similarly to the preparation of XIII, 4 g. p-(MeO)2C6H4 treated with 5 g. XIIb in the presence of 7 g. AlCl3 in 100 cc. CS2, the mixture decomposed, filtered, and the residue washed with hot H2O and sublimed at 130-3°/0.02 mm. gave a small amount of 2,3-HO[2,5-(MeO)2C6H3CO]C6H3CO2H, m. 147-9°. XIIb (10 g.) condensed as above with excess p-ClC6H4OEt in the presence of 12 g. AlCl3 in cold CS2, the hydrolysis product extracted with Et2O, the extract washed with aqueous NaHCO3, and the Et2O and alkaline solns. worked up gave Me p-ClC6H4 diester of XII, m. 105-6° (giving a brown-green FeCl3 reaction), and acids XII and XIIa. Saponification of the ester by refluxing 4-6 hrs. with 2N HCl or 2N NaOH gave XII and p-ClC6H4OH. An attempt at Fries rearrangement gave mainly XII by saponification, and a small amount of p-chlorophenyl 2-hydroxyisophthalate, m. 172-5°, subliming at 125-30°/0.02 mm.

ED Entered STN: 22 Apr 2001

IT **103393-74-4**, Acetophenone, 4',4'''-methylenebis[2'-chloro-5'-

hydroxy-
(preparation of)
RN 103393-74-4 HCAPLUS
CN Acetophenone, 4',4'''-methylenebis(2'-chloro-5'-hydroxy- (6CI) (CA INDEX NAME)



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